BUREAU OF HYGIENE AND TROPICAL DISEASES.

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PLAGUE.

LEFROU (G.). Considérations étiologiques sur l'épidémie de peste de 1929 à Saint-Louis du Sénégal. [**Etiology of Plague in 1929 at St. Louis, Senegal.**]—*Bull. Soc. Path. Exot.* 1932. June 8. Vol. 25. No. 6. pp. 597–606.

In this epidemic there was no evidence that an epizootic among rats either preceded, was concurrent with, or succeeded it. Special attention was paid to the matter and captured rats were specially examined for possible plague infection. On the other hand, fleas were very abundant and especially the flea now known as *Synosternus pallidus* and formerly as *Xenopsylla pallida* [*ante*, p. 154]. The conclusion is then drawn that the epidemic was due to transmission of infection from case to case by fleas. *W. F. Harvey.*

GOBERT (E.). Le controle permanent de la peste en Tunisie. [**The Permanent Control of Plague in Tunis.**]—*Arch. Inst. Pasteur de Tunis.* 1932. Mar. Vol. 20. No. 4. pp. 456–469. With 6 figs. on 5 plates.

A description is given of the travelling motor laboratory for plague service, which permits of investigation being carried into the country. It is in the country that the conditions of propagation of plague are most complicated. The flea, for example, can retain plague bacilli in its stomach for months* and ticks can act as vectors as well as fleas. Camels are known to suffer from plague and to be the starting point of epidemics. Man likewise can be the chronic carrier of plague bacilli. Research work is being carried on to determine the distribution of species of rodents and of the parasites which infest them. *W. F. H.*

PIQUET (L.). La peste dans le département de Constantine et plus particulièrement histoire de la peste bubonique à Philippeville et de la peste pulmonaire à Mac-Mahon, Barika, Condé-Smendou et Ain-M'lila, en 1930 et 1931. [**Plague in the Department of Constantine. History of Plague in Algeria in 1930 and 1931.**]—*Rev. d'Hyg. et de Méd. Préventive.* 1932. Mar. Vol. 54. No. 3. pp. 183–201.

This is an epidemiological and historical study in which it is claimed that striking demonstration has been afforded of infection passed from man

* La puce, par exemple, peut conserver les bacilles pesteux dans son estomac pendant des mois entiers (p. 464).

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and ceasing when contact ceased. This cessation is explainable if the human flea is unable to preserve its infecting power for so long a time as the rat flea. *W. F. H.*

LAMBERT (L.). La peste à l'hôpital central indigène en 1931. [**Plague at the Central Native Hospital (Dakar) in 1931.**]—*Bull. Soc. Path. Exot.* 1932. June 8. Vol. 25. No. 6. pp. 671–672.

Out of the 247 plague patients admitted 128 had been vaccinated more than a month, 10 less than a month and 109 had not been vaccin. ated at all. The mortality among the vaccinated was 37·5 per cent- and among the non-vaccinated 52·2 per cent. All the patients were treated by bacteriophage. *W. F. H.*

VAN DEN BERG (W. J. ROOS) & VOS (J. J. Th.). Klinische en pathologisch-anatomische waarnemingen bij pestgevallen te Bandoeng. [**Clinical and Anatomo-Pathological Observations on Plague at Bandoeng.**]—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1932. Apr. 12 & 26. Vol. 72. Nos. 8 & 9. pp. 465–478; 531–562. With 2 text figs. & 14 figs. on 7 plates. [20 refs.]

This paper concerns 66 cases of plague which were seen in the hospital at Bandoeng in 1929 and 1930 (3 cases observed in 1931 are mentioned in an appendix). The fatality was 50, or 76 per cent. Those who recovered (16) all had been suffering from bubonic plague. The chances of recovery appeared to be somewhat better in men than in women and decidedly better (32·5 per cent. against 8 per cent.) in individuals from 10 to 40 years of age than in children and older people. There were 51 cases of bubonic plague, 2 of plague ulcers, 12 of septicaemic plague and 1 of primary pulmonary plague. For the detailed analysis of the clinical observations and for the numerous case reports, quoted in the text, the original paper should be consulted. The treatment applied was purely symptomatic.

The anatomo-pathological part of the article is founded upon the experience obtained in 38 complete post-mortem examinations. In doubtful cases the autopsy may be helpful in order to establish the diagnosis though the last word is with the bacteriologist. Like other pyogenic organisms the plague bacillus may cause local affections at the "porte d'entrée" (sometimes the lung), as well as metastatic affections of the lymphatic system or by the way of the blood current. Its predilection for the lymphatic system and the typical character of the recent plague bubo are more or less specific. The haemorrhagic type of adenitis is rarely found in other diseases.

In judging whether a bubo is primary or secondary (by haematogenic metastatic spread) the author largely depends upon the stage of inflammation of the gland coupled with his knowledge of the duration of the illness. *W. J. Bais.*

VEDDER (A.). Rattepest aan boord van een stoomschip in de haven van Amsterdam. [**Rat Plague on a Steamer in Amsterdam.**]—*Nederl. Tijdschr. v. Geneesk.* 1932. May 14. Vol. 76. No. 20. pp. 2339–2347. With 3 figs. on 1 plate. English summary.

There have been 8 previous occasions on which plague has been found in rats on board ships arriving in Amsterdam. The strain isolated from this, the ninth, case presented certain peculiarities, in particular

that it was little virulent for guineapigs. One of the difficulties in the case of the rat is to distinguish *Past. pestis* from *Past. pseudotuberculosis rodentium.* The distinction is made by the test of cultivation in litmus-salt-peptone water tubes containing 0·5. 0·25, 0·1 and 0·05 per cent. glucose. All the tubes are turned red with growth but, whereas in the case of the former organism they remain red, in the case of the latter the 0·05 per cent. tube turns blue again after some days. The resemblance of the different types of colony forms (F-, G-, D-form) in the case of the two organisms is also discussed. By the criterion laid down the organism found on this occasion was a true plague organism. Its lack of virulence may have been due to the fact that its type of colony was one of comparative non-virulence. *W. F. H.*

LEFROU (G.). Contribution au diagnostic *post-mortem* de la peste. Les cadavres pesteux à foie négatif à l'examen direct. [**Post-Mortem Diagnosis of Plague.**]—*Bull. Soc. Path. Exot.* 1932. May 11. Vol. 25. No. 5. pp. 399–404.

The diagnosis was made within twelve hours of death and related to 323 cases, men, women and children suspected of plague. Of those who had palpable inguinal or axillary glands, 135 gave positive smears from both liver and gland, 26 positive liver and negative gland, 28 negative liver and positive gland, and 47 negative liver and negative gland, while of those without palpable glands 60 gave positive and 27 negative liver smears. The conclusions reached from the investigation are that:—(1) Simple needle puncture will not furnish, with certainty, smears that are positive; it is necessary to take a piece of the organ itself for the preparation of the smear. (2) Liver smears may be positive when gland smears are negative and *vice versa*; it is necessary to take smears from both if palpable glands, which are usually present in any case in the negro, are available. *W. F. H.*

OTTEN (L.). **The Problem of the Seasonal Prevalence of Plague.**—*Jl. Hygiene.* 1932. July. Vol. 32. No. 3. pp. 396–405. With 3 charts in text.

The seasonal prevalence of plague, with due regard to the existence of other possible factors, is due "almost exclusively to atmospheric conditions with their unmistakable influences on the flea. . . ." It has already been found that saturation deficiency affords a better correlation with plague periodicity than does relative humidity, after temperature has been taken into account. Fluctuations of temperature and humidity have a powerful influence upon flea prevalence and thus produce an effect, first upon the epizootic and then upon the epidemic. Saturation deficiency, however, will not wholly or satisfactorily explain seasonal fluctuation of plague. In Java there is a pronounced change of monsoons, but the temperature remains at a very uniform level. The author's researches go to show that it is the driest period of the year, that is to say in the third quarter, when increase of plague begins and that the peak is attained in the last months of the year. The wet monsoon lasts from November to April and the dry monsoon from May to October. By the second quarter of the year plague has reached its lowest point. In the mountainous parts of Java the flea index fluctuates closely with the seasonal course of plague, although it is not yet clear how relative humidity influences the development and viability of the flea in these regions. It is found moreover, that while there is

close correlation between the flea index and saturation deficiency, this is of an exactly opposite type to that which holds for British India.

W. F. H.

FONQUERNIE (J.). Sur deux cas de peste pulmonaire à longue évolution. [**Two Cases of Pneumonic Plague of Long Duration.**]—*Bull. Soc. Path. Exot.* 1932. Feb. 10. Vol. 25. No. 2. pp. 176–177.

The rapidly fatal issue of pneumonic plague was already recognized by GUY DE CHAULIAC in the Avignon epidemic of 1348 when he said "Et isti moriebantur intra tres dies." The duration of 50 hospital cases now recorded by the author is, within 24 hours 22, 24 to 48 hours 18, and over 48 hours 12. The great majority of those living more than 48 hours were dead within 3 days but two cases lived for 7½ days and 10 days respectively. *W. F. H.*

BULLETIN OFFICE INTERNATIONAL D'HYGIÈNE PUBLIQUE. 1932. Mar. Vol. 24. No. 3. pp. 438–499.—Enquête sur les résultats de la vaccination antipesteuse. Réponses au questionnaire : Egypte [pp. 441–6] ; Inde Britannique [pp. 447–56, 457–8, 459–78, 479–89, 490–3, 494] ; Italie [pp. 495–7] ; Maroc [pp. 498–9]. [**Enquiry into the Results of Plague Vaccination by Questionary. Replies of Egypt, British India, Italy and Morocco.**]

The points investigated, set out in the form of questions, were :—

A. (1) Method. Proportion of population vaccinated. Control population.
(2) Vaccination performed at the beginning, end, middle epidemic, or interepidemic period.
(3) Incidence upon the population at risk—isolated cases, numerous cases or dense foci.
(4) Reality of the Vaccination.

B. (1) Vaccine used. Composed of freshly isolated or old, very virulent or moderately virulent strains. Preparation—solid or liquid medium ; temperature of sterilization ; addition of antiseptics ; menstruum ; special characters.
(2) Concentration of germs.

C. (1) Number of injections and spacing.
(2) Doses.
(3) First appearance of immunity and its relation to the statistics of the vaccinated. Negative phase condition ; duration of immunity after one or more injections.
(4) Degree of reaction, local, regional and systemic. Correlation between reaction and immunity.

D. Results.

The replies to these questions are given in greater or less detail by each of the four countries mentioned and will doubtless be analysed after all the replies have been published. *W. F. H.*

FONQUERNIE (J.). Considérations sur un cas de longue incubation de peste pulmonaire. [**Long Incubation of Pneumonic Plague.**]—*Bull. Soc. Path. Exot.* 1931. Dec. 9. Vol. 24. No. 10. pp. 904–906.

A man, 66 years of age, who died in 8 hours from pneumonic plague in the quarantine station, had been removed from contact with a case of septicaemic plague 10 days before he showed any symptoms. Thus the incubation period is calculated to have been one of 10 days or longer.

W. F. H.

NAIDU (B. P. B.) & AVARI (C. R.). **Bacteriophage in the Treatment of Plague.**—*Indian Jl. Med. Res.* 1932. Jan. Vol. 19. No. 3. pp. 737–748. [8 refs.]

A powerful plague bacteriophage obtained from a rat, was capable of lysing a 24-hour growth of *Past. pestis* in less than two hours. Trials of this 'phage were made both in experimentally infected animals and man. In neither case were the trials effective in preventing death. A combination of 'phage and an anti-plague serum " resulted in a lesser number of recoveries from plague than what followed the use of the serum alone." *W. F. H.*

NAIDU (B. P. B.) & SATHE (R. G.). **" Germanin " (" Bayer 205 ") in the Treatment of Plague.**—*Indian Jl. Med. Res.* 1932. Jan. Vol. 19. No. 3. pp. 749–759. [47 refs.]

No evidence of bactericidal action of " Germanin " *in vitro* could be obtained nor was it found to possess any curative value when tested upon experimentally infected rabbits. *W. F. H.*

DE SMIDT (F. P. G.) **A Note on Laboratory Diagnosis of Plague Infections.**—*East African Med. Jl.* formerly *Kenya & East African Med. Jl.* 1932. Apr. Vol. 9. No. 1. pp. 2–13.

The bacteriological, the microscopic and the macroscopic diagnosis of plague is described in some detail. In puncturing a bubo it is essential to obtain by aspiration gland substance and " not merely the oedematous tissue or fluid surrounding it." If suppuration of the bubo has taken place it may not be possible to find plague bacilli in the pus. If plague bacilli are contained in sputum they are usually present in very large numbers so as to leave no doubt about the diagnosis. In order to get with certainty characteristic bipolar staining in films the author recommends Gram staining after alcohol fixation. *W. F. H.*

FRANCIS (Edward). **Duration of Viability and Virulence of *Bacillus pestis*.**—*Public Health Rep.* 1932. June 10. Vol. 47. No. 24. pp. 1287–1294.

The strain used was isolated from a California ground squirrel. Tests were applied for viability in the following cases :—No. 1 an agar culture which had remained sealed for 9 years at 10°C. ; No. 2 an agar culture which was subcultured at 3-monthly intervals for 9 years with other stock cultures and stored at 10°C ; No. 3 the whole spleen of a plague guineapig kept at –15°C. for 7 years and No. 4 a culture isolated from that same guineapig suspended in glycerine, stored at –15°C. and tested at intervals. The results were that No. 1 was viable and fully virulent, No. 2 viable and non-virulent, No. 3 viable and fully virulent and No. 4 fully virulent for 14 months, slightly virulent for 2 years 7 months and dead at the end of 3 years. *W. F. H.*

NAIDU (B. P. B.) & SATHE (R. G.). **The Comparative Value of Anti-Plague Bilivaccine and Haffkine's Plague Prophylactic.**—*Indian Jl. Med. Res.* 1932. Apr. Vol. 19. No. 4. pp. 987–992.

The bilivaccine was administered, according to directions, orally while Haffkine's plague prophylactic vaccine was given subcutaneously

in the test animals (rabbits) in a dose of 4 cc., as recommended for man. As a result of these experiments on rabbits the authors found no protection conferred by the bilivaccine as against 100 per cent. protection given by the subcutaneously administered plague prophylactic vaccine.

W. F. H.

SCHÜTZE (Harry). **Studies in *B. pestis* Antigens: I. The Antigens and Immunity Reactions of *B. pestis*. II. The Antigenic Relationship of *B. pestis* and *B. pseudotuberculosis rodentium*. III. The Prophylactic Value of the Envelope and Somatic Antigens of *B. pestis*.**—*Brit. Jl. Experim. Path.* 1932. June. Vol. 13. No. 3. pp. 284–288. With 1 fig.; pp. 289–293. With 1 fig. [10 refs.]; pp. 293–298. With 5 figs.

I. At an incubator temperature of 37°C., but not at 20°C., gelatinous envelopes, which are demonstrable in Indian ink preparations, make their appearance round all plague bacilli. As these envelopes never develop round *Past. pseudotuberculosis rodentium*, the character is a diagnostic one. By heating at 60°C the gelatinous envelope can be dissolved and used as antigen. A suspension of culture grown at 26°C, killed at 60°C and centrifuged, provided a supernatant fluid rich in somatic substance. It was discovered that gelatinous substance was heat-labile, haptenized in 15 minutes and destroyed in 60 minutes at 100°C. The somatic substance is stable. These two substances were used to furnish antisera and were found to be distinct antigens.

II. The heat-stable somatic antigen of *Past. pestis* is also possessed by *Past. pseudotuberculosis rodentium* and is " the basal rough framework of the bacillus, which . . . is laid bare and comes into action in an agglutination test only when the organism loses its smooth specific somatic factor and becomes rough. . . ." *Past. pseudotuberculosis rodentium* is motile and possesses (1) flagellar antigen, (2) a somatic antigen, which may be regarded as smooth, type-specific, and (3) the common rough somatic antigen. In the view of the author *Past. pestis* possesses ordinarily only a rough somatic antigen and no smooth species-specific antigen.

III. Important investigations have been made on the basis of the previous findings into the efficacy of plague vaccines. It is shown that, no matter what the medium used, prophylactic potency is enhanced to the extent of 50 to 100 per cent. by incubation of cultures at 37°C instead of at 26°C. As the former temperature is that at which gelatinous envelopes are produced in greatest abundance, it is reasonable to suppose that the envelope is what is efficacious prophylactically, especially as heating for 15 minutes at 100°C, which haptenizes envelope substance, renders a plague vaccine useless. An additional advantage gained by incubation at 37°C. is that the resultant broth vaccine is not only more potent but less toxic. *W. F. H.*

COUVY (L.), LAMBERT (L.) & DUFOUR (V.). Le principe lytique transmissible, dit " bactériophage " du bacille d'Yersin. [**The Lytic Principle or Bacteriophage of Plague.**]—*Ann. Inst. Pasteur.* 1932. May. Vol. 48. No. 5. pp. 541–593. With 12 text figs. [33 refs.]

Great stress is laid upon the specificity of the plague bacteriophage which necessitates the use of the 'phage appropriate to the particular

organismal type. Virulent 'phages are obtained by cultivation on single organismal strains. As it is not possible to identify the organismal type before use of the 'phage it is obviously necessary to use as polyvalent a 'phage as possible for treatment. Very encouraging results and comparatively little in the way of complication have been obtained in the treatment of plague. As patients do not appear for some days after attack a preliminary de-sensitization, by the subcutaneous injection of their own blood (autohaemotherapy), has been the routine practice in order to overcome the effect of the antiphage, which has presumably developed by that time. In bubonic cases the bacteriophage is administered subcutaneously and into the bubo in doses of 2 to 3 cc. on the first day and again on the second day, subcutaneously only on the third day. In septicaemic plague 3 cc. have been given intravenously in the course of 24 hours, repeated if necessary in 3 days time.

W. F. H.

Couvy (L.). Sur le bactériophage du bacille de Yersin. [**Plague Bacteriophage.**]—*C. R. Soc. Biol.* 1932. May 6. Vol. 109. No. 15. pp. 1344–1346.

The specific action of plague bacteriophage, isolated from the stools of convalescents, is illustrated by means of examples. A given 'phage lysed No. 1 strain in 3 hours and No. 2 in 3½ hours. It was cultivated in 4 passages with No. 2 strain and was exalted in virulence to the extent of being able to lyse this strain completely in 1¼ hours: it now took 5 hours, however, to lyse No. 1 strain and the lysis was followed by the development of secondary colonies. In another case a 'phage, which was lytic for several strains, lost by cultivation with one of these all its lytic power for the others. Still another experiment showed that a 'phage whose virulence had been exalted for one strain remained inactive towards strains which had originally been resistant to its action. These resistant strains, nevertheless, are not necessarily insensitive to 'phage action but require to be cultivated with their own specific 'phage in order to be lysed. The author concludes that the specific character of a bacteriophage has no relation to smoothness or roughness of colonies nor to S and R characters of the organism. The bacteriophage is strictly specific *in vitro* and if an apparent polyvalent action is shown it will disappear by cultivation with a single organismal strain. It is contended, therefore, that strains of plague bacillus are not to be regarded as identical in their reaction to 'phage unless both are still lysed in the same degree after cultivation of the 'phage in serial passage with one strain only. The bearing of these facts on the therapeutic use of bacteriophage has to some extent been confirmed in practice. Obviously, a 'phage in which a number of types is represented will be more likely to be active than one with only a single type, however potent it may be. The therapeutic action of the pestiphage is a function of the specificity of the lytic principle used.

W. F. H.

Couvy (L.). Le bactériophage du bacille de Yersin; son comportement *in vivo*. [**Plague Bacteriophage** *in Vivo.*]—*C. R. Soc. Biol.* 1932. May 13. Vol. 110. pp. 38–41.

In the first place the author affirms the perfect safety of treatment of plague by bacteriophage. Even intravenous administration gives

rise at most to slight shock and that but rarely. Its effect is rapid. Delirium quickly subsides ; on the following day pain has disappeared and in a few days the periadenitis is dispersed. If the bubo suppurates healing is obtained in 4 to 8 days after incision. Plague bacilli, which are abundant in gland juice obtained by puncture, are found to be in a state of lysis 2 hours after injection of 'phage. Some striking cases of bubonic plague have been cured in a few hours. Again, in cases of plague in which death has occurred in spite of treatment, it was not possible to obtain cultures of the plague bacillus from any of the organs *post mortem.* *W. F. H.*

PONS (R.). Le bactériophage anti-pesteux *in vivo.* [**Plague Bacteriophage in Vivo.**]—*C. R. Soc. Biol.* 1932. May 27. Vol. 110. No. 18. pp. 184–186.

Some of the findings of the author are that :—(1) Bacteriophage subcutaneously injected is rapidly generalized and produces in twenty-four hours a lysis of germs everywhere which, however, may not be complete. (2) In grave septicaemias injection of a lytic principle precipitates a toxaemia. (3) As long as lytic principle is demonstrable, cultures from either bubo or blood remain negative. (4) If during forty-eight hours the patient receives no bacteriophage, cultures from bubo or blood become positive if the illness has a fatal issue and remain negative in cases of recovery. *W. F. H.*

PONS (R.). Le bactériophage anti-pesteux *in vivo* chez l'homme, chez le cobaye et chez la souris. [**Pestiphage in Vivo in Man and Laboratory Animals.**]—*Bull. Soc. Path. Exot.* 1932. May 11. Vol. 25. No. 5. pp. 437–447.

After injection of bacteriophage the blood and fluid of buboes give no culture of plague ; the bacteriophage masks the infection. Therapeutically bacteriophage in somewhat doubtful instances appears to check the development of the disease. In the great majority of cases, however, and under the conditions of experimentation here employed, the bacteriophage was devoid of therapeutic action. No parallelism could be found between persistence of bacteriophage in the organism and the progress of infection. The infection might be fatal even though bacteriophage was demonstrable during the whole course of the disease and even at death. *W. F. H.*

ADVIER (M.). Existence d'un principe lysant le bacille de Yersin dans le sang d'une convalescente de peste. [**Plague Bacteriophage in the Blood.**]—*C. R. Acad. Sci.* 1932. Apr. 18. Vol. 194. No. 16. pp. 1397–1399.

PONS (R.) & DURIEUX (C.). Existence dans le bubon d'un pesteux convalescent d'un agent de la lyse transmissible, en dehors de sa présence dans l'intestin. [**Plague Bacteriophage in Bubonic Fluid.**]—*Ibid.* pp. 1399–1400.

A blood culture and the juice from an enlarged groin gland gave a growth of *Pasteurella pestis,* which subsequently dissolved away. An investigation of this phenomenon showed that it was due to the presence of the specific transmissible lytic principle for plague bacilli, and furnished proof that this principle could be found in situations other than the faeces. *W. F. H.*

ADVIER (Marcel). Caractères d'un principe lysant le bacille pesteux retiré du sang humain. [**A Lytic Principle for *P. pestis* in Human Blood.**]—*C.R. Soc. Biol.* 1932. May 27. Vol. 110. No. 18. pp. 161–163.

A bouillon blood culture from a plague convalescent, who had recovered without treatment, furnished a growth in six days which then disappeared in some hours by lysis. At the time when the growth appeared subcultures were made into bouillon and into agar. The bouillon cultures remained absolutely clear and successive passages were made, after a week's interval, to other bouillon tubes. These remained perfectly clear, but the lytic principle had nevertheless been transmitted in the subcultures and without loss of activity. It could lyse a suspension of plague bacilli in twelve hours and was perfectly specific. The subculture, which had been made on to agar, showed only a few isolated colonies of very slow growth. When these colonies were transferred to bouillon it remained clear, but showed high lytic power, strictly specific and transmissible. *W. F. H.*

SUGINO (Tameji). **On the Bacteriophage against the Plague Bacillus.**—*Kitasato Arch. Experim. Med.* 1932. Feb. Vol. 9. No. 1. pp. 72–81.

A plague bacteriophage was obtained from three laboratory strains of the bacillus. It was found to have a high degree of specificity, for it proved inactive even to allied organisms of the pasteurella group. Resistant strains to the bacteriophage were also developed.

W. F. H.

BOKALO (A.), WEDISCHTSCHEW (S.), SABININ (A.), JEGOROW (A.) & GRIKUROW (W.). Ueber Symbiose des *B. pestis* und des *B. pseudotuberculosis rod.* Pfeifferi mit Sarzinen. [**Symbiosis of *Past. pestis* and *Past. pseudotuberculosis rodentium* with Sarcinae.**]—*Zent. f. Bakt.* I. Abt. Orig. 1932. July 6. Vol. 125. No. 1/2. pp. 32–37. With 2 figs.

Weak suspensions of *Past. pestis* do not grow when sown upon agar plates, in which respect they differ from *Past. pseudotuberculosis rodentium.* If, however, citron-yellow, white or rose-yellow sarcinae be sown with the plague bacillus it is stimulated to grow.

W. F. H.

CHINESE MEDICAL JOURNAL. 1932. Apr. Vol. 46. No. 4. pp. 429–435.—Plague in Shansi and Shensi.

CHOLERA.

WU LIEN-TEH. **Report on the Cholera Outbreak of Shanghai 1931.**—*Reports National Quarantine Service Ser. II—1931.* pp. 70–86. With 9 text figs.

Shanghai appears to have had, during the past ten years, at least an outbreak of cholera every year. With better notification and laboratory diagnosis since 1930 no true case of cholera has been missed. The population of Shanghai is over 3,100,000. In the outbreak reported 482 cases occurred between the dates 8th August and 23rd October. The epidemic was of a very diffusely distributed character. It is at least noteworthy that not one of the 482 cases had received anti-cholera vaccination and that among 761,279 persons inoculated no instance of cholera infection could be traced. *W. F. Harvey.*

LOPEZ RIZAL (L.), SIAN (Jose) & PUNSALANG (Jose V.). **Cholera Epidemic in Bantayan.**—*Monthly Bull. Philippine Health Serv.* 1931. Oct. Vol. 11. No. 10. pp. 533–551. With 1 folding chart.

This investigation of the serious epidemic in Bantayan in 1930 has led the authors to the findings that :—(1) Epidemics of cholera have been occurring in the town since 1902, as shown by records. (2) The number of carriers among contacts was 1·61 per cent. as compared with 0·49 per cent. in the general population. (3) The recovery rate among the vaccinated cases was 61·39 per cent. and for the unvaccinated 45·45 per cent. (4) The endemicity of the infection is due to carriers. *W. F. H.*

DUGUET. Les épidémies de choléra au Hedjaz. [**The Epidemics of Cholera in the Hedjaz.**]—*Rev. Prat. Malad. des Pays Chauds.* 1931. Nov. 10th Year. Vol. 11. No. 11. pp. 492–495.

"Cholera has always been the scourge of pilgrimages. . . . and . . . the Hedjaz is the post of relay of cholera in its progress from the Far East towards the West." There have been twenty-seven Hedjaz epidemics in the last eighty-one years. Cholera is as frequent in winter as in summer and would seem to be endemic there, either because of continuous introduction from external sources or as a result of recrudescence at the time of pilgrimage. On the return journey from Mecca pilgrims making their way back to Egypt and the Mediterranean are isolated at Tor, where they undergo disinfection and a quarantine detention for three to five days. This station, therefore, to which cholera has been carried fulfils the function of a barrage. Much work remains to be done, and that by the bacteriologist, before the question whether imported cholera is one of case or carrier can be settled.

W. F. H.

DE VOGEL (W. Th.). Sur l'identification du vibrion cholérique. [**Identification of the Cholera Vibrio.**]—*Bull. Office Internat. d'Hyg. Publique.* 1932. Feb. Vol. 24. No. 2. pp. 262–270. With 3 coloured figs. on 2 plates.

The isolation at El Tor by DOORENBOS in 1930 and 1931 of vibrios which were agglutinable by anticholera serum but were strongly

haemolytic, has raised anew the question which arose in 1905 regarding the vibrio El Tor. The circumstances are identical. There was no cholera among the pilgrims. The regulations, however, which apply in the event of the outbreak of cholera, were put into force and have elicited strong protest. The position is very much as it was originally, except for the fact demonstrated by VAN LOGHEM, that while the El Tor vibrio is haemolytic both have the power of digesting haemoglobin and producing a transparent zone when grown on a blood-agar medium. The opinion is expressed that this culture reaction is a significant one and differentiates El Tor and saprophytic vibrios from the cholera vibrio. It is very desirable that the position of the El Tor vibrio should be definitely settled. *W. F. H.*

VAN LOGHEM (J. J.). De El Tor-vibrio. [**The El Tor Vibrio.**]—*Nederl. Tijdschr. v. Geneesk.* 1932. Apr. 23. Vol. 76. No. 17. pp. 1939–1948. With 1 coloured plate. [22 refs.] English summary (5 lines). [Summary appears also in *Bulletin of Hygiene.*]

The author reaffirms the necessity for distinguishing, in the case of vibrios, between haemodigestion and haemolysis and between exo- and endohaemolysin. The erythrocytes of the guineapig and the rabbit are too sensitive for these tests. Sheep or goats' blood should be used. If a true cholera vibrio at a late stage of growth appears to haemolyse blood this is due to autolysis of the vibrios and the action of endohaemolysin. A true haemolysin is a product of living bacteria: it acts early and not late in growth, is thermolabile and antigenic. These are characters which differentiate it from the endohaemolysin. That the cholera vibrio has digestive action is shown by its ability to digest casein and to liquefy gelatin. It can, naturally, also digest blood and it is this property which gives rise to the greenish zone around a stroke blood-agar culture. Spectroscopic investigation shows the disappearance of blood pigment with digestion in the transparent zone around a cholera growth. In the case of the transparency brought about by haemolysis the blood pigment is still present. The bearing of these facts upon the controversy over the identity of the El Tor and the cholera vibrios, which has been raised again by the isolation at Tor of the same type of vibrio from pilgrims not suffering from cholera, is this:—

1. The true cholera vibrio is haemodigestive but not haemolytic.
2. The El Tor vibrio is both haemodigestive and haemolytic.
3. Both these vibrios are morphologically and serologically identical.

W. F. H.

VAN LOGHEM (J. J.). Der El Tor-Vibrio. [**The El Tor Vibrio.**]—*Ztschr. f. Hyg. u. Infektionskr.* 1932. June 23. Vol. 114. No. 1. pp. 20–30. [20 refs.]

The whole El Tor vibrio question may be said to have been raised anew with the discovery 25 years later of the same organisms, under the same conditions of a cholera-free pilgrimage and in the same place. It might be said that the question is now a purely academic one, but it is not so, for on the official diagnosis of cholera during this pilgrimage will depend the verdict as to infected ports and the quarantine and disinfection of large groups of persons. Van Loghem's own contribution to the subject, which is not a recent one, was the distinction

which he drew between haemodigestion as a peculiarity of the cholera vibrio and the marked haemolytic action of the El Tor vibrio. It is now, as he says, all-important to settle whether (1) a non-haemolytic strain of vibrio can become haemolytic and (2) a haemolytic strain can be the cause of cholera. *W. F. H.*

DOORENBOS (W.). Étude sur la symbiose du vibrion cholérique avec le bactériophage. Reproduction expérimentale des variations des caractères biologiques des vibrions cholérigènes. [**Symbiosis of the Cholera Vibrio with the Bacteriophage. Experimental Production of all the Possible Variants of the Cholera Vibrio.**]—*Ann. Inst. Pasteur.* 1932. Apr. Vol. 48. No. 4. pp. 457–469.

With the appearance of this paper the long drawn out controversy whether haemolytic El Tor vibrios are true cholera vibrios, bids fair to come to an end. This may be best explained by means of the conclusion arrived at, which is that " it is possible by the agency of the bacteriophage of d'Herelle to transform *in vitro* the agglutinable vibrio into a non-agglutinable, the non-haemolytic into the haemolytic, the vibrio giving a feeble indole reaction into an indole-producer and to isolate from one and the same strain of vibrio organisms which are agglutinable and organisms which are non-agglutinable, haemolytic and non-haemolytic."

It is the presence of bacteriophage in the cultures that is the chief cause of modification of the distinctive characters by which the true cholera vibrio is recognized. In fact, the El Tor vibrio is a cholera vibrio contaminated with bacteriophage. The former is an endemic and the latter the epidemic type of cholera vibrio. *W. F. H.*

KIRIBAYASHI (Shigeru) & AIDA (Toshiro). **Experiments with " Yatren 105 " on Cholera-Carriers.**—*Taiwan Igakkai Zasshi* (*Jl. Med. Assoc. Formosa*). 1932. May. Vol. 31. No. 5 (326). [In Japanese. English summary p. 53.]

Yatren 105 of strength 0·1 per cent. in distilled water and 0·5 per cent. in normal salt solution and peptone water killed cholera vibrios within 1 hour, 1 hour and 12 hours respectively. Given to seven carriers in doses of 1·5 to 2·1 gm. per day *per os* it caused disappearance of the vibrios within 2 to 5 days. *W. F. H.*

DE RAYMOND (A.). Note thérapeutique sur le traitement des diarrhées cholériformes et éventuellement du choléra. [**Treatment of Choleriform Diarrhoea and of Cholera.**]—*Bull. Soc. Path. Exot.* 1932. Mar. 9. Vol. 25. No. 3. pp. 196–199.

The therapeutic method here advocated is one of intravenous injection of very hypertonic solutions of chloride. It is based on the idea that what is required is not merely the temporary restoration of the chlorides lost in such a disease as cholera, but the arrest of their withdrawal from the tissues. The method has been used with success in intestinal occlusion and consists in intravenous injection of a combined solution of 30 per cent. sod. chloride and 2 per cent. gonacrine daily. The amounts used are two injections daily of 10 to 20 cc. of the salt solution and one injection of 5 cc. gonacrine. Gonacrine is added

for its action on the toxaemia of infection. Altogether 22 cases of choleriform diarrhoea were treated with the death of only 2 instead of the usual 60 to 80 per cent. *W. F. H.*

RICOU & TRAN-VAN-TAM. Premier essai de traitement du choléra en Indochine par l'immuno-transfusion sanguine. [**First Attempts at the Treatment of Cholera by Immuno-Transfusion of Blood.**]—*Bull. Soc. Méd.-Chirurg. Indochine.* 1931. Nov.-Dec. Vol. 9. No. 10. pp. 795–799. With 1 folding chart.

The type of cholera case which is commonly received into hospital with imperceptible pulse, a temperature in the mouth of 86°F., black and viscid incoagulable blood, retracted eyeballs, and glazed cornea and not a drop of urine passed in twenty-four hours is not going to be saved by any form of therapeutic intervention. And so it was in the cases of immuno-transfusion here recorded. The method of treatment is interesting, although so far ineffective. Healthy group-4 blood donors with no taint of syphilis, tubercle or leprosy were chosen and received 4 injections at 6 days interval of cholera vaccine subcutaneously in the doses 1, 2, 3 and 4 cc. They were ready to supply blood after the 2nd injection and received a dose of 1 cc. cholera vaccine intramuscularly before each transfusion. The transfusion procedure used was that of glucose serum and amounts of 150 to 200 cc. were administered daily without any mishap. *W. F. H.*

PANDIT (C. G.) & RAO (R. Sanjiva). **A Note on the Type of Cholera Bacteriophage isolated from Cases during a Small Epidemic of Cholera in Madras.**—*Indian Jl. Med. Res.* 1932. Apr. Vol. 19. No. 4. pp. 1019–1021.

A smooth strain of cholera vibrio was used, which was uncontaminated with 'phage. From this strain a rough variant was obtained by ordinary dissociation methods. The three cholera 'phage types A B and C were made to act upon the smooth strain to give secondary colonies and these secondary colonies were tested for antigenic structure along with the original smooth strain and its rough variant. The appropriate sera were obtained by immunization of rabbits. Somatic antigen showed the main change. This antigen was considerably diminished in the case of secondary A, but it persisted in varying amounts with secondaries B and C. The above gradation was noted in the case of flagellar antigen also. The power to provoke normal agglutinins was found to be proportional to the amount of somatic antigen present. *W. F. H.*

PANDIT (C. G.) & RAO (R. Sanjiva). **A Note on the Antigenic Structure of Secondary Cultures obtained with the Three Types of Cholera 'Phages and a Strain of Cholera Vibrio.**—*Indian Jl. Med. Res.* 1932. Apr. Vol. 19. No. 4. pp. 1023–1028.

This is an account of the isolation of an " A " type of cholera bacteriophage, capable of lysing a representative strain of each of the four groups of Indian cholera vibrios at present known. It is contended by the authors that this 'phage A was not the result of natural propagation of that 'phage contained in a mixture of A, B and C types which had been administered in the Infectious Diseases Hospital four months previously. *W. F. H.*

PASRICHA (C. L.), DE MONTE (A. J.) & GUPTA (S. K.). **A Preliminary Note on New Types of Cholera 'Phage—Types D. & E.**—*Indian Med. Gaz.* 1932. May. Vol. 67. No. 5. pp. 262–264. With 5 figs. (2 on 1 plate).

The isolation from water of a 'phage " W " to cholera-like vibrios, the secondary growths of which were lysable by true cholera 'phage, caused the authors to search for new types of cholera 'phage other than the A, B and C types already differentiated. These new types, it was supposed, would link up the A, B and C types with the newly isolated bacteriophage. The authors possessed filtrates of cholera stools and water samples to the number of 550 with which to try out this hypothesis. A type D has now been definitely isolated and " evidence is presented to show the existence of one other or perhaps two other (E and F) types of cholera 'phage." The D 'phage shows what is called reciprocal action. This is equivalent to saying that type A cholera 'phage lyses the secondary cultures of the types B, C and D cholera 'phage ; B 'phage those of A, C and D ; C 'phage those of A, B and D ; and D 'phage those of A, B and C. *W. F. H.*

MESNARD (J.) & GENEVRAY (J.). Contribution à l'étude du vibrion cholérique. [**A Variant of the Cholera Vibrio.**]—*Arch. Insts. Pasteur d'Indochine.* 1931. Oct. No. 14. pp. 51–62. With 1 coloured plate.

Recently isolated strains of *Vibrio cholerae,* which were being used for preparation of vaccine showed alongside the typical moist, bluish, translucent, colonies with well defined margin, other colonies which were smaller, dry, white, opaque with more or less regular margins and a wrinkled surface. These were not contaminations, nor are they considered to be even a mutation of the cholera vibrio. They are variants with the same characters as the normal cholera but differing in degree. The characters of the wrinkled colony vibrios, as contrasted with normal colonies are :—slower in the digestion of gelatin and coagulated serum, more vigorous in fermentation of glucose and saccharose, less proteolytic and less indologenic, much more haemolytic, less pathogenic and less agglutinogenic. After intraperitoneal injection of guineapigs with vibrios from wrinkled colonies, the cultures made from the peritoneal fluid showed mostly colonies of normal type.

W. F. H.

PASRICHA (C. L.), DE MONTE (A. J.) & GUPTA (S. K.). **Mutation of Cholera Vibrios. (The Characters of the Population of a Freshly-isolated Cholera Colony, with a Note on Some Colony Variants of Cholera and Cholera-like Vibrios.)**—*Indian Med. Gaz.* 1932. Feb. Vol. 67. No. 2. pp. 64–69. With 3 text figs.

Bile-salt agar medium was used to obtain the variant dissociated colonies. The tests applied were, microscopic examination of colonies, Millon's reaction for roughness and smoothness, agglutinability with standard cholera serum and lysability by the 3 types of bacteriophage. With repeated cultivation and selection, colonies were obtained differing from the parent colony in morphological, serological and cultural

characters. Inagglutinable and partially agglutinable colonies, for example, could be obtained from a good agglutinating colony. Some colonies lost likewise their agglutinogenic power.

W. F. H.

RUSSELL (A. J. H.). Un essai d'application du bactériophage à la prévention du choléra. [**Trial of Bacteriophage in the Prevention of Cholera.**]—*Bull. Office Internat. d'Hyg. Publique.* 1932. Feb. Vol. 24. No. 2. pp. 271–273. With 1 text fig.

In this communication regarding a still unfinished trial of bacteriophage a graph is given of the epidemic incidence of cholera in two noted centres, one in which the treatment was afforded and one in which it was not. The result is significantly in favour of bacteriophage, but two years are still to run before publication of results, so as to exclude the possibility that the cessation of cholera was due to simple and temporary decrease.

The use of the mixed dysentery-cholera bacteriophage for all cases of diarrohea and dysentery at the quarantine camp of El Tor is recommended and evidently the recommendation is being carried into practice. *W. F. H.*

MADRAS PRESIDENCY. REPORT OF THE DIRECTOR OF PUBLIC HEALTH, MADRAS, FOR 1930. pp. 12–18. With 1 map & 2 graphs.—**Cholera.**

A considerable sum of money was voted by the Madras Government to test the protective value of bili-vaccine against cholera. The great advantages of this vaccine are that it does not require to be administered by a medical man and that being given orally, it is more popular than subcutaneous vaccine. The chief difficulty in connexion with its use is that it must be given on three successive days and before any food is taken. It is unfortunate for the trial that the cholera epidemic was exceptionally mild and that several villages where no vaccine was administered also escaped infection. The results cannot be looked on as final and conclusive. *W. F. H.*

NGUYEN-VAN-KHAI. Contribution à l'étude de la prophylaxie du choléra par la vaccination anticholérique. (Résultats constatés de 1926 à 1930 dans la province de Tan-An.) [**Results of Prophylactic Vaccination against Cholera.**]—*Bull. Soc. Méd.-Chirurg. Indochine.* 1932. Feb.-Mar. Vol. 10. No. 2. pp. 175–186.

The method of vaccination used was a single dose of 3 cc. where it was difficult to recall the persons vaccinated for a second dose. It is considered that at least 48 to 72 hours are required before immunity is established and that 5 to 7 days are necessary before it can be taken as certain. In the absence of any other efficacious method anti-cholera vaccination is regarded as one of the best measures available against cholera. The yearly vaccinations are tabulated. *W. F. H.*

MALARIA.

BARBER (Marshall A.), RICE (Justus B.) & BROWN (James Y.). **Malaria Studies on the Firestone Rubber Plantation in Liberia, West Africa.**—*Amer. Jl. Hyg.* 1932. May. Vol. 15. No. 3. pp. 601–633. With 1 plan & 2 figs. [11 refs.]

This experiment was carried out on small groups of labourers isolated in new clearings in the jungle. Anopheline density was very high, about 4 per cent. were infected, and the human parasite rate was 80 per cent. The usual anti-mosquito measures, by draining and the like, were impracticable, and therefore the effect of plasmoquine was tried, each person being given a dose of one centigram twice a week. A great fall in the sporozoite rate of the local anopheles followed this treatment, with no corresponding fall in the control camps. In the most isolated group under treatment, no mosquitoes infected with sporozoites were found among 1,478 dissected over a period of 22 days. A striking feature was the rapid rise in the öocyst rate which occurred 14 days after the plasmoquine had been discontinued. Through natural or acquired resistance the labourers were comparatively free from severe illness. A more balanced diet would probably lower the parasite rate and diminish sickness from all causes. "To eradicate malaria from any large portion of such a plantation would be next to impossible." If treatment with plasmoquine is to be successful, "the group to be treated should be more or less isolated from non-treated groups, and should be amenable to treatment." (See also this volume, p. 359.) *W. Fletcher.*

SERGENT (Etienne). Les épidémies de paludisme et la météorologie en Algérie. [**Epidemic Malaria and Meteorology in Algeria.**]—*Bull. Soc. Path. Exot.* 1932. Feb. 10. Vol. 25. No. 2. pp. 133–136. With 2 graphs.

Epidemics of malaria have occurred every 12 years since 1902. The curve showing the yearly rainfall between November and June, and the curve of the sunspots' area, follow, to a certain extent, the same line as the malaria curve. The most important cause of an epidemic in the summer is heavy rain and flooding in the spring.

W. F.

i. DE FEYTER (C.). Résultats des recherches des indices splénique et hématologique chez les enfants indigènes de Chinkolobwe (octobre 1931). [**Splenic and Parasitic Indices of Native Children at Chinkolobwe.**]—*Ann. Soc. Belge de Méd. Trop.* 1932. June 30. Vol. 12. No. 2. pp. 225–226.

ii. ESTAS. Recherche des index splénique, gametien et malarien sur la population infantile des camps de Jadotville en octobre 1931. [**Splenic and Gametocyte Indices of Children at Jadotville.**]—*Ibid.* pp. 227–228.

iii. REYNTJENS (Paul). La malaria chez la population infantile du camp indigène de Lubumbashi en novembre 1931. [**Malaria among Native Children at Lubumbashi.**]—*Ibid.* pp. 229–239.

i. In 100 children between the ages of 2 and 10, the splenic index was 56, the parasite index 82, and the gametocyte index 42.

ii.	0–2 yrs.	2–10 yrs.	10–15 yrs.
Total.	234	310	241
Splenic Index ...	24	41	16
Parasite Index ...	82	98	92
Gametocyte Index ...	41	79	44

iii. Among infants 3 months old, 19·5 per cent. were infected. At two years the maximum of 86·6 is reached. In places where the maximum degree of infection is reached very early one concludes that the degree of endemicity is very high; where the maximum is reached at a later age, the endemicity is lower. *W. F.*

RASMERITZA (E.). **Malaria in Roumania.**—*Riv. di Malariologia.* 1932. Vol. 11. No. 1. 12 pp.

Malaria has been endemic along the Danube and its affluents for hundreds of years. An experimental survey was begun by CANTACUZENE in 1904, and prophylactic quinine was given in nine rural areas. Only 0·09 per cent. of the treated persons suffered from malaria, but 11·4 per cent. of the untreated. All work was interrupted by the war, and malaria greatly increased. Malaria control at the present time is carried on by the Ministry of Public Health through some 1,200 officers. The technical work is in charge of a special commission composed of 13 members, including the three professors of hygiene. The treatment of carriers is given each year between January and April, when the new generation of anopheles appears; the health officers locate and treat the acute cases; free distribution of quinine was begun in 1923; quinine, arsenic and iron are prepared in the laboratory of the Ministry of Public Health; blood and spleen examinations are compulsory and are made by the health officer of each area. "Both the incidence and gravity of the disease have decreased. . . . The effect is slight, however . . . quinine control of the disease is expensive, and is not a definitive measure." *W. F.*

SARATHY (M. K. P.). **Observations on Malaria in Puri District, Orissa.**—*Indian Med. Gaz.* 1932. May. Vol. 67. No. 5. pp. 254–260. With 2 charts & 1 map.

There is much malaria on the shores of Chilka Lake, the large inland sea of Orissa which is connected with the Bay of Bengal. *A. fuliginosus* is the prominent species in the area, and was the only anopheles found infected by the author. It breeds in the paddy fields. *W. F.*

WATSON (Malcolm). **Studies in the Parasitology of Malaria in the Federated Malay States between 1900–1912.**—*Indian Jl. Med. Res.* 1932. Apr. Vol. 19. No. 4. pp. 1209–1224. With 1 chart. [15 refs.]

KNOWLES and SENIOR-WHITE stated in their "Studies in the Parasitology of Malaria" (this *Bulletin*, 1931, Vol. 28, p. 612) that the parasitological aspects of malaria appeared to have been almost completely ignored in the F.M.S. The author quotes numerous records from annual reports and local medical publications to refute this accusation. An interesting suggestion is that anti-malaria sanitation may alter the relative proportions of the three species of parasites. Between the years 1907 and 1910, among 4,430 cases

examined in Singapore, 75 per cent. were subtertian, 16 simple tertian, and 5·4 quartan. Anti-malaria work was begun in 1911, and the results were excellent. The relative proportions of the different species among 5,284 cases, examined in 1915–1928 were: subtertian 40 per cent., simple tertian 57, quartan 2. *W. F.*

MOOIJ (W.). De malariabestrijding te Tanahmerah, Bovendigoel van 1 Maart 1930 tot 1 Maart 1931. [**The Malaria Campaign at Tanahmerah, Bovendigoel, from March 1, 1930 till March 1, 1931.**]—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1932. Jan 15. Vol. 72. No. 2. pp. 66–82. With 4 charts & 1 plan.

Tanahmerah (Dutch New Guinea) is a place of exile for political convicts. The malaria rate has risen since 1927, subtertian being most prevalent. The highest rate regularly occurred during the rainy season. *A. punctulatus, var. moluccensis* and *A. bancrofti* have been recognized as the vectors. The first was found breeding in open pools and drains and in shallow spots on the banks of the river and various brooklets. The breeding places of *A. bancrofti* were unknown.

The author divides the period of his activity into three parts:—

(1) From March till the end of June 1930. This was a rainy season. Yet the malaria morbidity, especially the subtertian rate, showed a marked drop, which in view of the experience in previous years can only be ascribed to the systematic quinine and plasmoquine prophylaxis, which is described in detail.

(2) The dry season from the beginning of July till the end of November 1930, was as such favourable for the malaria campaign. The influence of measures taken during this time (quinine and plasmoquine prophylaxis and oiling) cannot be estimated.

(3) From the beginning of December 1930 till the end of February 1931, a rainy season again, the malaria rate was much lower than could be expected in view of previous experience, which must be ascribed to the systematic antimalarial campaign. The influence of the completion of the draining system before the beginning of this period must also be taken into account.

The breeding places of *A. bancrofti* have now been discovered, being shaded, shallow parts of the river and various small currents in the jungle round the camp. *A. bancrofti* having pronounced anthropophilic habits the imagos from long distances may be attracted by human settlements. In view of the inaccessibility of the breeding places their treatment appears impracticable. *W. J. Bias.*

SOUTHERN MEDICAL JOURNAL. 1932. May & June. Vol. 25. Nos. 5 & 6. pp. 521–551; 642–667. With 1 fig. & 1 map. [55 refs.]—**Symposium on Malaria, Part 1.** [8 papers.] **Part 2.** [7 papers.]

This symposium comprises papers read before the National Malaria Committee at New Orleans in November 1931. The chairman, Dr. S. S. COOK, spoke of malaria in Haiti, where the people lived as did their primitive African ancestors until the National Public Health Service was created in 1919; since then much has been accomplished, but malaria cannot be satisfactorily controlled under existing economic and political conditions. *A. albimanus* is the vector, and its larvae can be found below 2,500 feet in almost every kind of water deposit. Dr. C. C. HOFFMANN read a paper on malaria in Mexico with special

reference to *A. pseudopunctipennis*. Along the coast, *A. crucians* breeds in the brackish water of the mangrove swamps. *A. albimanus* is found along the rivers, from their mouths up to about 1,200 feet. *A. quadrimaculatus* occurs in the northern part of the country, both on the coast and in the interior. In the high arid plateau, *A. pseudopunctipennis* is the carrier. The only rivers of this region rise in the high mountains, and on reaching the hot plains they sink underground. Very clear waters rise in the beds of these rivers ; they run for about a hundred yards, and then sink under the ground again ; sometimes the springs form small pools. The anopheles breed in this water, and also in fountains, wells and tanks in the towns. In the valley of Mexico City, at an altitude of 7,200 feet, both *A. quadrimaculatus* and *A. pseudopunctipennis* are present.

Dr. G. H. Bradley reported his observations on the breeding requirements of anopheles in Louisiana. The abundance of larvae was not greatly affected by variations in the mean summer temperature. A certain amount of floating algae was necessary to protect them from the top water minnows, but too much prevented their breeding. No consistent differences were found between the plankton of breeding and non-breeding waters. The hydrogen-ion concentration of the waters containing larvae did not differ from that of those which contained none. The examination of gut contents did not throw much light on the matter.

Dr. W. Krauss reported on the analysis of 8,354 cases of therapeutic malaria inoculation in 68 institutions. The percentage of deaths was 5·38. The object of the study was to determine the reason for the high death rates. He urged the importance of a perfect hospital organization and a better knowledge of malaria. Dr. Bruce Mayne preferred infection by means of mosquitoes to the inoculation of blood, and instanced fatalities due to blood being taken from a donor with a latent septicaemic infection in one case and, in another, to the donor having an undetected infection with subtertian parasites. He keeps his mosquitoes at about 76°F. while sporozoites are developing, and subsequently at 38° to 40°F. They are shipped, when required, in a portable refrigerator at 38·F. The sporogonic cycle is checked below 60°F., and the gametocytes taken with the host's blood either fail to exflagellate or gametogenesis is rendered innocuous, but low temperatures have no ill effect when the sporozoite stage has been reached.

Drs. H. C. Clark and W. H. W. Komp described observations made in some rural villages of the Republic of Panama. "Measures in malaria control seldom include the treatment of that vast number of rural people who really form most of the seed bed of malaria." Practically the whole population was infected, and they propose to inaugurate mass treatment with quinine and plasmoquine which, to be successful, must be under thorough discipline.

Dr. M. A. Barber spoke of malaria in West Africa (see this volume p. 331). By means of oil and Paris green, he and a colleague controlled the breeding of anopheles in an area with a radius of half-a-mile round the Rockefeller yellow fever laboratory at Yaba, near Lagos, and they extended their operations about one mile to windward, but the malaria danger was not materially reduced, because anopheles came in from outside the protected area. "Malaria control work in West Africa must take into account a wide dispersion range of *costalis*. . . . Screening is not likely to become general in West Africa. Few white people except Americans use it extensively."

Dr. E. C. FAUST stated that while satisfactory decreases had occurred in the malaria mortality rate in some places, there were still extensive areas where the rate was essentially the same as it was 10 years ago. Dr. F. L. HOFFMAN considered that progress was being made gradually. His paper contained several interesting tables, one of which is reproduced here.

Malaria Death Rates in Different Localities, 1919–1929.

Rates per 100,000 estimated population.

India.

Year	Calcutta.	Ahmedabad	Bangalore	Bombay	Bareilly
1919	132·5	567·7	55·5	23·1	—
1920	143·9	875·2	74·4	26·9	—
1921	133·7	839·4	60·5	45·5	25·2
1922	118·9	564·0	66·4	40·4	102·4
1923	117·8	410·7	90·8	33·0	89·8
1924	145·0	595·5	39·5	39·4	95·7
1925	186·7	480·7	47·1	46·1	88·9
1926	155·3	986·0	18·5	49·6	93·1
1927	135·5	1007·9	13·5	28·1	167·8
1928	124·9	1071·2	6·7	22·7	161·9
1929	86·1	1440·5	5·9	16·6	130·1

Year	Kingston, Jamaica	Trinidad & Tobago	San Juan, Porto Rico	Havana, Cuba	U.S. Reg. Area
1919	46·3	262·1	19·9	5·2	3·8
1920	35·0	222·2	27·2	5·4	3·6
1921	52·6	242·2	27·0	6·1	3·6
1922	19·0	225·3	17·1	9·2	3·6
1923	23·4	201·4	9·3	7·5	2·8
1924	40·0	199·2	15·5	4·1	2·5
1925	80·9	206·3	12·7	4·8	2·1
1926	33·1	209·7	20·2	4·2	1·9
1927	29·8	167·1	12·6	2·9	2·7
1928	39·7	218·1	14·7	4·1	3·5
1929	14·5	161·9	10·8	1·4	3·6

W. F.

RAYNAL (Jean). Note sur le paludisme d'altitude. [**Malaria at High Altitudes.**]—*Marseille-Méd.* 1932. Feb. 25. Vol. 69. No. 6. pp. 245–260. With 4 figs.

Guatemala City is situated in a central plateau at an altitude of 5,000 feet surrounded by lofty mountains. These highlands were free from malaria until about 1930, when malaria broke out suddenly in epidemic form. Its appearance is attributed to the return to their highland home of labourers who had been working on the sugar or banana estates down near the coast. The carrier in the highlands is *A. pseudopunctipennis*, and the malaria is benign tertian, though on the coast, where the labourers became infected, subtertian predominates. The reasons for this are, probably, that *P. falciparum* does not develop so well in either man or mosquito in the cold hills as it does in

the warmer plains, and that *A. pseudopunctipennis* is not such a good carrier of *P. falciparum* as *A. albimanus* and *A. argyrotarsis*, which are the anopheles of the plains. *W. F.*

RUSSELL (Paul F.). **Malaria. An Account of its Cause, Cure and Prevention. Prepared especially for the use of Students and Teachers in the Philippine Islands.**—*Bureau of Science Popular Bull. 10.* 62 pp. With 34 text figs. & 1 plate. 1931. Manila. Bureau of Printing.

The students and teachers of the Philippines are to be congratulated on having been provided with this most interesting booklet on malaria. It begins with an outline of the history of early investigations, with full-page photographs of the pioneers, LAVERAN, MANSON, ROSS, and GORGAS. The cause, transmission, predisposing factors, symptoms, diagnosis, and control of malaria are dealt with in various sections, and there are excellent illustrations. As the book is intended for Philippine students it deals almost exclusively with the Philippine anophelines. It will be noted that *A. funestus minimus*, the carrier, breeds only in the foothills. The lowlands are not malarious ; nor are the mountains, for *A. minimus* is not found above 1,800 feet. Dr. Russell writes, on p. 45, " It may be stated definitely that quinine as a prophylactic drug is a failure." But he admits its value as an emergency measure, and writes that it " is at present the only practical method of maintaining the efficiency of temporary expeditions into regions where malaria is severe." *W. F.*

MISSIROLI (A.). Tipi epidemici delle febbri malariche. [**Epidemic Types of Malaria.**]—*Riv. di Malariologia.* 1932. Jan.-Feb. Vol. 11. No. 1. pp. 1–24. With 10 plates. [14 refs.] English summary p. 133.

Though based on a relatively small number of examinations (the inhabitants of Posada in Sardinia, where the investigation was carried out, amounted to 750) this article is of considerable interest. CELLI has distinguished three epidemic types of malaria in Europe : (1) The North-Europe type—nearly all benign tertian, early developing into epidemicity in the spring, very rarely quartan and never subtertian. (2) The Northern Italy type—benign tertian predominating, least in February and March, steadily increasing through the spring and summer and rapidly decreasing in the autumn. (3) The Southern Italy type—marked preponderance of subtertian, usually of high degree of virulence ; least prevalent from February to June, sharp and rapid rise in July lasting throughout the summer, falling in the autumn, rapidly or slowly, according to meteorological conditions. The article is illustrated by several charts and tables from which it is seen that in Posada subtertian malaria diminishes from January to June, begins to develop epidemicity a month after the rise in the anopheline curve, attains a maximum in July, falls very slightly in August and rapidly in September and October. It is thus of the Southern Italy type of CELLI.

The charts and tables show that in the pre-epidemic stage there is a large number of crescent carriers, and it is due to these that malaria can occur although anopheles are relatively few. The author finds that benign tertian (in the sub-tropical zones) is largely a disease of

early childhood, becoming progressively rarer after the age of 12 years; that immunity acquired against *P. vivax* is more solid than that against *P. falciparum* after repeated infections by the corresponding plasmodium. He maintains that the benign tertian observed in the spring in Posada is a recurrence of the infection of the previous year, and explains the subtertian prevalence over benign in July and August as due to "the greater receptivity of larger numbers of the population" [this appears more tautological than explanatory].

Swelling of the spleen was observed to be less after the epidemic season in children below 5 years, owing to intensive treatment, but the reduction was barely perceptible in those between 6 and 12 years and imperceptible above that age; finally, the parasitic index taken just after the epidemic period, when quinine has been properly employed, is remarkably low and does not give a proper idea of the gravity of epidemic or endemic malaria. *H. H. S.*

HACKETT (L. W.) & MISSIROLI (A.). **Housing as a Factor in Malaria Control.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1932. June 30. Vol. 26. No. 1. pp. 65–72.

Certain houses, notorious for malaria and known as "malaria houses," are supposed to be especially attractive to mosquitoes, because they are dark and damp, and consequently offer such an ideal shelter that the insects remain indefinitely, or return after every flight, and eventually infect the whole household. These "malaria houses," as distinguished from houses which are malarious because they are near a breeding place, are not important in themselves, the authors have never come across one in all their experience, but they have assumed a fictitious importance because on them has been built the theory that a chief factor in malaria is the attractive shelter afforded to anopheles, by dark, damp houses, and that the disease can be prevented by providing better houses and raising the standard of living. The authors' observations do not support this theory, for it is their experience that good housing or bad housing has little bearing on the fact that in one region anopheles enter houses, and in another they do not. For example, in North Germany, round Emden, the people are more prosperous, keep more cattle, and are better housed than the inhabitants of Baden, in the south; yet malaria is endemic in the north, while it has disappeared from Baden in spite of the apparently equal number of anophelines in both places. At Valdichiana, which used to be intensely malarious, and where the inhabitants still live in ancient, dark, ill-ventilated dwellings, the anophelines do not come into the houses, and there is no malaria. In such places the anophelines seek the cow-sheds instead of the houses. In Fiumicino, on the other hand, where the houses are light and new, and where there are stables under the same roof, 25 per cent. of the mosquitoes caught on the premises were in the bedrooms. Several other examples are given (see the same authors, this *Bulletin*, 1931, Vol. 28, p. 569).

There is no good evidence to show that the lingering of a mosquito in the place where it has fed is an important factor in its becoming infective and causing new cases. While some vectors, such as *maculipennis* and *quadrimaculatus*, may remain in a house for a day or two, others, such as *maculatus*, leave after biting. The authors' experiments with stained anopheles did not show that there was any tendency for

them to return to the place where they had previously fed. *Maculipennis* in some regions seeks human habitations, in others it seeks stables. This difference in behaviour has nothing to do with the character of the houses or the stables, but is due to the anopheles in one district being of a different race, with different feeding habits, from the anopheles in another (see DE BUCK, SCHOUTE and SWELLENGREBEL *ante*, p. 345). One race (*A. maculipennis labranchiae* Falleroni) lays a grey dappled egg. It is relatively more prevalent in dwellings than the second race, and both in northern Europe and Italy there is a certain parallelism between the prevalence of this race and the incidence of malaria. The second race (*A. maculipennis messeae* Falleroni) lays an egg irregularly pigmented in bars and patches. It predominates in non-malarious areas, frequents stables more than dwellings, and goes into complete hibernation in winter. In certain regions it bites only animals and is completely dissociated from man. The phenomenon of "anophelism without malaria" is bound up with the food preferences of this barred-egg race, and not with housing standards. The authors have seen no satisfactory evidence of this kind in connexion with any species except *A. maculipennis*. It is indeed certain that nothing of this kind occurs in the case of *A. costalis*.

In a malarious locality the principal effort should be directed at screening the houses and destroying breeding places. More intensive agriculture and more cattle may, in *maculipennis* areas, favour the ascendancy of an innocuous race of insects. *W. F.*

SCHÜFFNER (W. A. P.), SWELLENGREBEL (N. H.), ANNECKE (S.) & DE MEILLON (B.). Vergleichende Untersuchungen ueber Malaria-immunität in Niederländisch-Indien und Südafrika. [**Comparative Investigations on Malarial Immunity in Dutch East Indies and South Africa.**]—*Zent. f. Bakt.* I. Abt. Orig. 1932. July 6. Vol. 125. No. 1/2. pp. 1–31. With 12 graphs. [27 refs.]

The authors carried out investigations amongst Malays in hyperendemic malarial areas in Dutch East Indies and amongst Bantus in hyperendemic areas in South Africa with the help of methods, which in every particular, corresponded exactly, and they found that the adults had acquired an immunity against malaria. The immunity of the Malays they describe as parasitic immunity using ZIEMANN'S name for it; this immunity is not a result of an inherited tolerance. The degree of immunity is inversely proportional to the adult parasitic index. On the other hand, the malarial immunity of the Bantus is identical with the "premunition" of SERGENT. It is only acquired by races who possess an inherited tolerance to the malarial parasite. The degree is proportional to the percentage of adult "carriers" with few parasites. The important researches in India by CHRISTOPHERS are fully referred to. The paper is an important one and is illustrated by graphs. It should be consulted in original by malariologists and others interested in the subject. *E. D. W. Greig.*

JAMES (S. P.), NICOL (W. D.) & SHUTE (P. G.). **A Study of Induced Malignant Tertian Malaria.**—*Proc. Roy. Soc. Med.* 1932. June. Vol. 25. No. 8. pp. 1153–1186 (Sect. Trop. Dis. & Parasit. pp. 37–70). With charts.

Several workers have thought that the malignant tertian parasite, because it sporulates in the brain, might have a higher therapeutic effect than the other forms. Usually the risks are too great; but,

at Horton, specialist experience, expert laboratory control, and trained nursing provide effective safeguards against these risks, and the fatality rate is only 4 per cent. as compared with 10 to 14 per cent. attributable to courses with *P. vivax* in the mental hospitals of England and Wales.

Some of the strains used came from India, some from Italy, and some from West Africa. In any study of malignant malaria, a problem of great interest is whether there is more than one species of malignant parasite. The passage of different strains through series of patients and frequent examinations of the blood of all cases did not enable the authors to detect any noteworthy morphological differences between them. They also found that the fever associated with all strains had a true tertian periodicity and was due to groups of parasites which sporulated every 48 hours. In many cases the fever appears to be irregular or quotidian ; this is due to the presence of several groups of parasites sporulating at different times so that before one paroxysm has subsided, another is treading on its heels. It is a remarkable feature of malignant malaria that three or more groups of parasites are present. This is one of the chief reasons why malignant malaria is more severe than benign tertian where there are never more than one or two groups. The authors therefore conclude that there is no reason to postulate the existence of a quotidian parasite.

It has often been said that infections with *P. falciparum* in one place are more serious and difficult to cure than infections with the same species in another place ; in this respect, the authors found that there was a wide difference between their strains ; and they concluded that " there are various geographical races which, while not being morphologically different, can be recognized as being distinct by their clinical virulence, immunological reactions and other biological properties." The infections produced by the Roman strains were much more severe than those produced by the Indian strains, and it took about eight times as much quinine to control the primary attack. The fever periods lasted twice as long in infections with the Roman strains, and the relapses extended over a much longer period than with the Indian strains. There were 16 cases in the Indian group and none of them lasted longer than eleven weeks. In the Roman group, there were only 11 cases, but 7 of them lasted more than twenty-one weeks, and two of them developed blackwater fever.

There were also immunological differences as shown by the fact that a patient who had become immune to an Indian strain, as the result of repeated infections, was yet highly susceptible to infection with a Roman strain. Still another difference between the Indian and the Roman strains is the constant failure to infect European *A. maculipennis* with the Indian strains, though they are readily infected with the Roman strains. The reason why a given species of anopheline is a good carrier in one country and not in another, may be that the strains of parasites in the latter have no capacity to infect this particular anopheline.

Long incubation periods of six months or more, such as are sometimes seen in benign tertian malaria, have not been observed in malignant tertian ; the longest incubation at Horton, after a mosquito-bite infection, was 17 days ; the shortest was 6 days, and the mean was 12 days.

In benign tertian (see James *et al*, this *Bulletin*, Vol. 28, p. 566), apart from the recrudescences and relapses which occur in the first

24 weeks, 30 per cent. of the patients have a recurrence about 35 weeks after the date of infection. This does not happen in malignant tertian, in which the febrile attacks seldom occur after 24 weeks. Clinically it consists of a severe primary attack followed by several less severe recrudescences; in benign tertian there are, in addition, much later manifestations, the "relapses" and "recurrences." Malignant tertian is an acute disease as opposed to benign tertian which is a chronic one. The recrudescences are so much milder than the primary attack, that it is only in the latter that there is grave risk, apart from blackwater fever; the parasite infection diminishes in each recrudescence. Parasites sometimes persist in the blood long after the last febrile recrudescence; parasites were present in 10 out of 54 cases from 7 to 159 days after the last febrile attack.

The following conditions must be taken into consideration in appraising the value of quinine and other drugs:—(1) The mode of infection. (2) The degree of susceptibility. (3) The tolerance or immunity acquired by reason of former attacks. (4) The species of parasite. (5) The virulence of the particular strain. (6) The dose of infection. Patients with naturally acquired malaria who are treated in hospitals for tropical diseases in non-malarious countries, have already suffered from primary attacks and have developed some immunity. They are simply suffering from recrudescences and are therefore easily cured. This is the chief reason why systems of treatment, based upon experience in non-malarious countries, fail when they are applied in the tropics where primary attacks have to be treated.

The degree of tolerance or immunity acquired has a great influence on the subsequent course of the disease, and is so quickly acquired that, as a rule, all risk is confined to the primary attack. "This being so, it seems clear that, whenever it is possible to do so, it is in the best interest of patients suffering from malignant tertian malaria to use quinine only very sparingly for the treatment of recrudescences . . . with the object of allowing the patient to acquire the tolerance which alone . . . seems to bring about permanent recovery." The authors conclude from observations that "the advice invariably given in text books to the effect that in malignant tertian malaria one must set about giving quinine as soon as the diagnosis is made, may not always be in the best interests of the patient."

Treatment by erion, now called atebrin. Seven patients were infected, all with the same strain, Rome 11, by means of mosquitoes. Five were treated with atebrin 0·3 gram daily for five days, and two were treated with quinine. The primary attack was quickly controlled; but the quinine-treated cases had numerous recrudescences, while those treated with atebrin had none. Several other patients were given atebrin; among them were four who had continued to relapse for more than six months after their primary attacks, and two of them had had blackwater fever; in each case there was a quick disappearance of fever and parasites, and no subsequent recrudescence. Fifteen cases in all were treated with atebrin, and in only one did it fail to effect a permanent cure. *W. F.*

GORDON (R. M.) & DAVEY (T. H.). *P. malariae* **in Freetown, Sierra Leone.**—*Ann. Trop. Med. & Parasit.* 1932. Mar. 19. Vol. 26. No. 1. pp. 65–84. With 1 map & 2 graphs. [2 pages of refs.]

The authors examined native children by the thick film method during the months February to September 1931. The examination

showed a great increase in quartan malaria as compared with other years. The only anopheles found in the houses were *A. costalis* (many) and *A. funestus* (few). They attempted to infect these mosquitoes, but without success. On reviewing the attempts of others to do this they found no unimpeachable evidence of success, and they state that "It seems a very surprising fact that the evidence regarding the transmission of *P. malariae* by anophelines should rest on such a small basis of fact." Malaria in children rises steeply to 40 per cent. at 18 months, the rate remains fairly constant to 13 years of age and then falls to 14 per cent. by 16 years. The commonest parasite in children between 3 and 14 years old was *P. malariae*. The percentages were :— *P. falciparum* 16·1 per cent. ; *P. malariae* 19·6 per cent. ; *P. vivax* 0·1 per cent. The proportion infected with malaria parasites was about 40 per cent. *P. ovale* Stephens was not found. *W. F.*

TOPORCOFF (T.). [**Epidemiology of Quartan Malaria.**]—*Trop. Med. & Vet.* Moscow. 1931. Vol. 9. No. 1. pp. 3–6. [In Russian. English summary.]

A study of the distribution and epidemiology of quartan malaria in Russia based on statistics for a period of five years (1924–1928). The prevalent idea that this type of malaria occurs in isolated foci was based on single examinations in separate localities and is not borne out by the present investigation. Quartan malaria was found to be evenly distributed in all parts of the country where malaria is prevalent, and the percentage of cases in relation to that of the other forms of malaria is fairly constant. A certain seasonal periodicity was observed, the incidence being the highest in the autumn and winter months.

C. A. Hoare.

LAMBERS (J. A. P. Hille Ris). Over quartana-nephritis en haar beteekenis in Suriname. [**On Quartan Nephritis and its Significance in Surinam.**]—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1932. Mar. 15. Vol. 72. No. 6. pp. 334–346. [14 refs.]

The connexion between quartan fever and nephritis is more and more generally recognized. Clinically the kidney affection is a combined nephrosis and nephritis, running a chronic course ; the prognosis as regards recovery is unfavourable.

The author's statistical research in Surinam (Dutch Guiana) reveals the following facts. Out of 28,000 hospital cases under 40 years of age there were 1,833 microscopically established cases of malaria (31 per cent. subtertian, 42 per cent. tertian, 12 per cent. quartan, 1 per cent. mixed 14 per cent. undefined). Out of 222 cases of quartan fever 109 had nephritis (49·1 per cent.), of the subtertian cases 3·8 per cent., of the tertian cases 5·3 per cent. Of 676 cases of nephritis 109 were caused by quartan malaria (16·8 per cent.). This characterizes quartan fever as a factor of real importance in the causation of nephritis in Surinam. Yet the author does not consider the connexion as a specific one, but (like GIGLIOLI) thinks that the benign character of quartan fever allows the patients to refrain from adequate treatment for a much longer period than they can stand in subtertian or tertian infections, so enabling the (quartan) malaria to exercise its nephritis-producing toxic influences on the system more effectively than in the other types of fever. *W. J. Bais.*

DAVIS (N. C.) & KUMM (H. H. W.). **Further Incrimination of *Anopheles darlingi* Root as a Transmitter of Malaria.**—*Amer. Jl. Trop. Med.* 1932. Jan. Vol. 12. No. 1. pp. 93–95.

Many malaria cases occurred among workmen and their families at Iranca, in Bahia, during February 1931. The predominant larvae in breeding areas were *A. albitarsis*, but the only anopheles caught in the houses were *A. darlingi* and 28·7 per cent. were infected out of 240 examined ; 7·4 per cent. showed sporozoites. *W. F.*

THONNARD-NEUMANN (E.). Plazentare Malariainfektion, kongenitale Malaria und Impfmalaria. [**Placental Malarial Infection, Congenital Malaria and Inoculation Malaria.**]—*Muench. Med. Woch.* 1932. Mar. 4. Vol. 79. No. 10. pp. 382–383.

The author considers that during the latent period the malarial parasite finds, in addition to the spleen, liver and bone marrow, the placenta very suitable as a temporary resting place. In Panama in coloured women it was found in the placenta in 7 per cent. of cases by CLARK, but in only 3 per cent. in the peripheral blood as well. The author in 1928 in Panama found a heavier infection, in 20 per cent. a positive finding in the placenta, but only 5 per cent. of the women showed a simultaneous peripheral blood infection. For the transmission of the infection to the foetus damage to the placenta is necessary. He states that he does not know whether in autopsies of cases of G.P.I. treated by malariatherapy plasmodia have been found in the spleen, liver or bone marrow, indicating that the parasites had merely been removed from the peripheral blood by the quinine treatment and the malaria had passed into a latent condition. [The reviewer has examined the brain, liver and spleen of several cases of G.P.I. being treated by B.T. malarial therapy and who died during or shortly after the course and has not been able to demonstrate malarial parasites in them. Both smears and sections were made.] *E. D. W. Greig.*

RUGE (Reinhold). Die Malaria-Therapie und Prophylaxe in ihrem Verhältnis zur Unfallversicherung. [**Malaria Therapy and Prophylaxis in Relation to Accident Insurance in Germany.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1932. May. Vol. 36. No. 5. pp. 253–260. [36 refs.]

The author takes as his text a government order of 1929, which schedules tropical diseases as occupational diseases for insured sailors. It reads as follows :—" Compensation can be claimed if a drug, which has been administered for the treatment of an occupational disease, causes damage which leads to loss of employment or death." He considers the various accidents which may occur in connexion with quinine adminstration, particularly quinine idiosyncrasy. He then discusses plasmoquine, which he favours for the curative and prophylactic treatment of malaria. As a result of his study he lays down the following dictum :—" For steamers trading to malarial coasts prophylaxis with the completely innocuous plasmoquine should be compulsorily introduced, and any one refusing this prophylaxis should forgo all accident benefits for malaria." *E. D. W. Greig.*

TOULLEC (F. L.). L'expertise du paludisme. [**Examination for Malaria.**]—*Marseille-Méd.* 1932. Jan. 25. Vol. 69. No. 3. pp. 97–105.

This paper is concerned with the examination of pensioners claiming benefit on account of malaria. Most authorities agree that malaria is soon cured after return to France. For example RIEUX states that a year or a year and a half is enough, and that he has never found parasites after two years. MARCHOUX has found none later than three years. There are, however, incontestable observations of relapses 6, 9, 13 and even more years after return from a malarious country, and these exceptional cases are rightly taken into consideration by legal authorities. Therefore all pensioners must be thoroughly examined and a scheme for their examination is set out in detail.

W. F.

ELDIN (M. Salah). **The Nature of Pulmonary Lesions in Malaria.**—*Arch. f. Schiffs- u. Trop.-Hyg.* 1932. May. Vol. 36. No. 5. pp. 260–275. With 5 text figs. [39 refs.]

The author concludes :—

" Malarial infection produces lesions in the lung, some of which can be attributed to the direct action of the parasite and its products : these are :—

"1. A proliferative congestive lesion of the alveolar walls was found constantly in 7 post-mortems. It usually occurs in chronic malaria tropica cases ; and it can produce the clinical picture designated. . . as 'intermittent malarial pneumonia'."

"2. Minute multiple infarcts were found in one case. . . ." [cf. DUDGEON & CLARKE 1918]

Some excellent micro-photographs are given. *W. F.*

HOLLAND (J. H.). **Ledger Bark and Red Bark.**—*Kew Bull. Misc. Information.* 1932. No. 1. pp. 1–17. [12 refs.]

This paper deals with the early history of Cinchona planting (see this *Bulletin* 1931, Vol. 28, p. 817). Only about one pound of the seeds which Ledger sent to England in 1865 were sold to Java ; the remaining 13 pounds were bought by Mr. J. W. B. Money, an Indian planter, who exchanged them for *C. succirubra* seed, with the Director of Cinchona Culture. The *Calisaya Ledgeriana* seeds were sown in the Nilgiri plantations, but they did not do well. The seed sown in Java, however, prospered excellently in the volcanic soil of the Preanger district. Though *C. succirubra* grows well in India, and has a high content of total alkaloids, its content of quinine is lower than *C. Ledgeriana* ; even when *Calisaya* is cultivated in India it does not yield nearly as much quinine as when grown in the more suitable soil of Java. Medical opinion has favoured the use of quinine to the exclusion of other alkaloids though it has been shown repeatedly that they differ little in therapeutic value ; the price paid for the bark depends therefore on its quinine content, and consequently no country has been able to compete with Java. Sir David PRAIN, speaking of the " monopoly," has said that it is not the creation of Java, but it is due to the fact that the quinine-producing *C. Ledgeriana* grows better there than anywhere else, and that quinine is prescribed to the exclusion of the other alkaloids. Various Commissions have reported in favour of the use of

the total alkaloids, and this will render easier the increased production which they recommend, because the hardier trees, such as *C. succirubra*, will flourish in many countries where *Ledgeriana* will not grow. Burma, Ceylon, Jamaica, Cameroons, Tanganyika, and British Malaya, are countries in which planting may be extended. Totaquina (see HENRY, below) is not the first standardized preparation of the mixed alkaloids; in 1923, the Government of Madras introduced a standardized preparation of cinchona febrifuge, under the name "Malarene," which gave excellent results. *W. F.*

DE VOGEL (W. Th.). Le "monopole" hollandais du quinquina. [**The Dutch Cinchona "Monopoly."**]—*Bull. Office Internat. d'Hyg. Publique.* 1932. Feb. Vol. 24. No. 2. pp. 278–290. With 1 text fig.

[An important paper by Dr. M. KERBOSCH which dealt with this question was summarized on p. 817, Vol. 28, 1931, of this *Bulletin*. The present communication deals with it from a rather different angle.] The convention between the planters and the manufacturers of quinine was suggested by the Government of the Dutch Indies in order to save the industry from the ruin which threatened it from the violent fluctuation in prices manipulated by financial speculators. In 1884, the price of quinine before extraction was 51 florins per kilogram. The cultivation of quinine was then encouraged by the Government, and seeds of the rich *Ledgeriana* were supplied to the planters; but from these seeds grew, not *Ledgeriana* which is itself a hybrid, but a mixed lot of trees, so poor in quinine that all calculations were upset and the planters were faced with serious losses. The Government came to their help, with knowledge obtained by careful experiment, and supplied them with cuttings from selected trees which were grafted on the stumps of those which they had originally planted. But when at last the planters put their bark on the market, they could only get a third of the price obtained in 1884, though the price of quinine after extraction and preparation in Europe had actually gone up. By 1896, the production of quinine had greatly increased and the price of the unextracted alkaloid had fallen to only a tenth of what it had been twelve years before. Ceylon planters were ruined and abandoned cultivation. The price of extracted quinine was disproportionately high, and so the planters of Java set up their own factory in order to escape the strangle hold of the manufacturers. The answer of the latter was to flood the market with quinine sold at a loss. Many plantations were then abandoned, less quinine was produced, and, in a couple of years, the price rose once more. This led to more planting which was followed by another slump, this time so severe that several planters sold their estates for a single florin on condition that the purchaser took over the liabilities.

It appeared to the Government that the only way to preserve the industry was by an agreement between the planters and the manufacturers regulating the supply in accordance with the demand, and regulating the price of the bark with regard to the price of quinine. The Government, which itself produces 10 per cent. of the total output of bark on its own plantations, subscribed to the arrangement only on condition that quinine should be supplied cheaply to places in need of it, and reserved the right of withdrawal should the convention impede the provision of the drug to malarious countries. In the early days

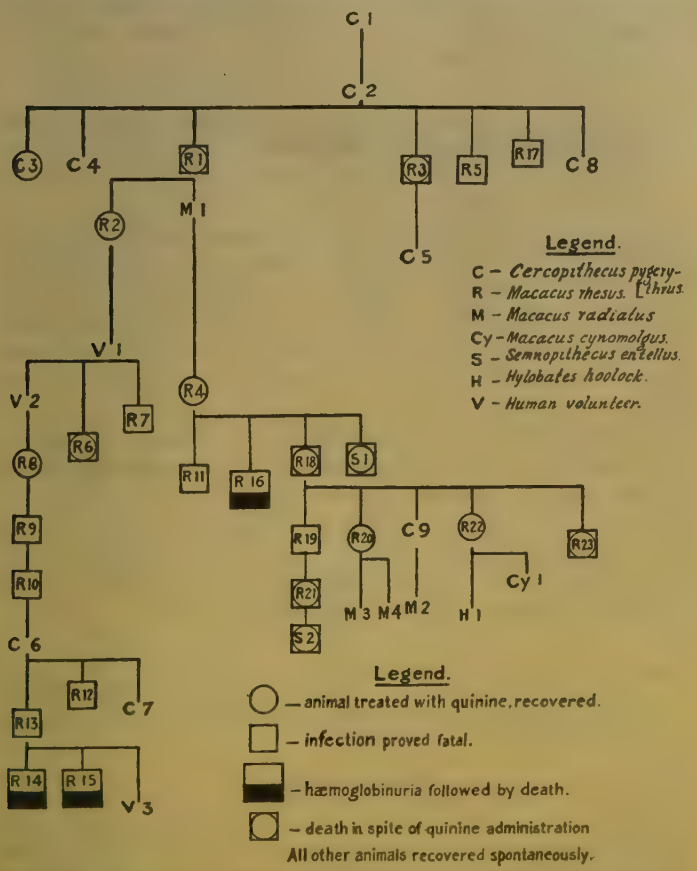
of the association the war broke out, communication between manufacturers in different countries was interrupted, and quinine once more fell into the hands of speculators. It was then that, according to Martindale and Westcott (*Extra Pharmacopoeia*), the Kina Bureau saved the situation by providing quinine at a reasonable price. That planters are not making a fortune by exploiting the needs of the sick is shown by the fact that there was a reduction of a thousand hectares of quinine in Java between 1929 and 1930. It has been said that the price of quinine, stabilized by the convention, is too high to allow of its purchase by the governments of malarious countries in quantities sufficient for their needs. A diagram is given depicting in black columns the total annual expenditure of several malarious countries such as Greece and Bulgaria, and, for comparison, the amount spent on quinine, and also the amount which would need to be spent in order to supply the drug to all who needed it. Even the latter expenditure would be an infinitesimal addition to the total budget. Again, why should Java be held responsible for a quinine shortage in other countries? Would the rice-producing countries, such as Burma and Indo-China, be blamed if there were a rice famine in Java? As a matter of fact the association has helped many foreign countries to supply quinine to their necessitous subjects, and, in April 1931, an offer was made to the Malaria Commission of the League of Nations to supply 500,000 kilogrammes of quinine annually at four-sevenths of the official price. The courage and persistence of the Dutch planters in the face of grievous losses, and the peculiarly suitable soil and climatic conditions of Java, have contributed to the success of cinchona cultivation in the country which now supplies 97 per cent. of the world's quinine, and only in this sense is it a monopoly. The association helps other governments who wish to cultivate cinchona by supplying them with plants and seeds, and also by putting their long experience at their disposal. Even in Java, planting is not restricted to the Dutch; there are many foreign planters, and the Italian Government owns a large estate in Java. The author has no doubt that the Government of the Dutch East Indies, by bringing about the agreement between the planters and the manufacturers, saved cinchona planting from extinction, and assured the quinine supply of the world. *W. F.*

NAPIER (L. Everard) & CAMPBELL (H. G. M.). **Observations on a Plasmodium Infection which causes Haemoglobinuria in Certain Species of Monkey.**—*Indian Med. Gaz.* 1932. May. Vol. 67. No. 5. pp. 246–249. With 1 chart.

A plasmodium resembling *Plasmodium kochi* was found accidentally in a monkey (*Cercopithecus pygerythrus*), whose health was unaffected. Other monkeys, both cercopithecus and *Macacus rhesus*, were inoculated with the blood of the first, and several further passages were made. The infection ran a mild course in the cercopithecus monkeys, but, in the macacus monkeys it was virulent, and 11 out of 12 of them died. Haemoglobinuria occurred in 8 of the 11 fatal cases. None of these 11 cases was treated with quinine; in other cases, in which quinine was given, there was no association between the occurrence of haemoglobinuria and the giving of quinine. The haemoglobinuria was always associated with heavy infection. The virulence of the strain, and the tendency to produce haemoglobinuria, appeared to increase with passage. *W. F.*

KNOWLES (R.) & GUPTA (B. M. Das). **A Study of Monkey-Malaria, and its Experimental Transmission to Man. (A Preliminary Report.)**—*Indian Med. Gaz.* 1932. June. Vol. 67. No. 6. pp. 301–320. With 7 plates (5 coloured), 6 charts & 1 graph.

This paper records the transmission of monkey malaria to man, and back again to monkey. An extremely scanty infection with a plasmodium was found in an African monkey, *Cercopithecus pygerythrus*, said to have been imported from Singapore; the strain was passaged into others of the same species and thus established in the laboratory; [NAPIER and CAMPBELL made their experiments with the same strain. See above.] In *C. pygerythrus* it caused a mild infection which disappeared spontaneously, or was readily cured by quinine. The parasites in this monkey resembled benign tertian; the corpuscles



Graph showing passages of virus of monkey-malaria. The vertical lines are proportional to the incubation periods (i.e. from inoculation to the first appearance of parasites in the inoculated animals).

[Reproduced from the *Indian Medical Gazette.*]

were swollen and Schüffner's dots were present. In *Macacus rhesus* it caused very severe infections. After about 5 days of fever the temperature fell suddenly and the animals died. There was intense anaemia with normoblasts, anisocytosis and basophilia. Parasites were present in enormous numbers, and in 3 monkeys out of 23 haemoglobinuria occurred just before death. The parasites did not disappear with the onset of the haemoglobinuria. The morphology of the parasites was completely changed by inoculation into this monkey. The corpuscles were not enlarged, there were no Schüffner's dots, and the ring-forms and rosettes resembled *P. falciparum*, though there were only 8 to 11 merozoites. The gametocytes resembled those of *P. malariae*. The infection was transmitted to three human volunteers by inoculation. In one the disease was mild, in another it was moderate, and in the third extremely severe. The infection was passaged back to monkeys, from two of these human cases. The morphology of the parasite in man was much the same as in rhesus monkeys, but there was a greater resemblance to *P. malariae* *W. F.*

GREEN (Richard). **A Malarial Parasite of Malayan Monkeys and its Development in Anopheline Mosquitoes.**—*Trans. Roy. Soc. Trop. Med. & Hyg.* 1932. May 14. Vol. 25. No. 6. pp. 455–477 With 2 plates (1 coloured) & 7 figs. [33 refs.]

A malaria parasite in the blood of monkeys was discovered by KOCH in 1898. LAVERAN gave it the name *P. kochi*. The author describes, with excellent illustrations, a parasite of the common Malayan macaque *Macaca irus*. The parasite resembles the benign tertian parasite of man, and is identified as *P. inui*; it occurred in a quarter of the monkeys examined. It persists for many months and the disease runs a benign course. *A. kochi*, *A. maculatus* and *A. vagus* became infected after feeding on parasitized monkeys, and the öocysts were indistinguishable from those of benign tertian. Culicines and monkey lice gave negative results. Attempts to infect monkeys by injecting sporozoites of *P. inui* and of *P. falciparum*, or human blood containing *P. vivax*, were unsuccessful. From the evidence available, it appears improbable that, in the ordinary course of events, man becomes infected with the malaria parasites of other primate families, but this point requires further investigation. The finding of öocysts or sporozoites in mosquitoes, within an area where there are monkeys, is not necessarily evidence of infection with human malaria. *W. F.*

ADANT (M.). Tentative d'inoculation du paludisme aux singes (*Plasmodium falciparum*). [**The Inoculation of Monkeys with** *P. falciparum*.]—*Ann. Soc. Belge de Méd. Trop.* 1931. Dec. 31. Vol. 11. No. 4. pp. 371–372.

Two *Cercopithecus subaeus* and two cynocephalus monkeys (one of each species having been splenectomized) were inoculated subcutaneously with 10 cc. of citrated blood heavily infected with *P. falciparum*. Frequent examinations were made for 30 days, but no parasites were found. Inoculations were repeated, using non-citrated blood rich in subtertian parasites and injecting it into the saphenous vein. Daily examination of the blood for 45 days was negative. Films made from spleen and liver puncture were also negative. *W. F.*

HUFF (Clay G.). **Further Infectivity Experiments with Mosquitoes and Bird Malaria.**—*Amer. Jl. Hyg.* 1932. May. Vol. 15. No. 3. pp. 751–754. [12 refs.]

There are four species of malaria, differing widely both morphologically and biologically, to which the domestic canary is susceptible:—(1) *Plasmodium relictum* Grassi and Feletti (often called *Proteosoma* or *Plasmodium praecox*), (2) *P. cathemerium* Hartman, (3) *P. rouxi* Sergent, (4) *P. elongatum* Huff. The first two have rounded gametocytes which displace the nucleus of the red cell; the other two have elongated gametocytes which lie alongside the nucleus. The importance of recognizing these different species is that the susceptibility of mosquitoes is not the same to all of them. A certain culicine may be readily infected with one but not with another. In reports of experiments with bird malaria, the species of parasite should always be specified. *W. F.*

i. DE FEYTER (C.). Contribution à l'étude du paludisme congénital. [**Congenital Malaria.**]—*Ann. Soc. Belge de Méd. Trop.* 1932. June 30. Vol. 12. No. 2. pp. 245–248.

ii. VAN NITSEN (R.). Le paludisme congénital.—*Ibid.* pp. 249–252. [21 refs.]

i. Six newly born babies were examined at the end of the dry season when anopheles were not breeding in the neighbourhood. Schizonts were found in three babies. The first was examined two hours after birth; the second, seven days after; the third was born dead at the sixth month, and parasites were found in its spleen and in blood from the cord. The mothers were infected in all three cases.

ii. Reviews the "literature" on the subject and concludes that congenital malaria is rare and only occurs when the placenta is damaged. *W. F.*

SENEVET (G.). Mécanisme de l'accès paludeen par le choc hémoclasique. Nouveaux faits à l'appui de cette thése. [**Haemoclastic Shock in the Mechanism of the Malarial Paroxysm.**]—Reprinted from *Sci. Méd. Assoc. Franc. pour Avanc. des Sci.* Algiers. 1930. pp. 336–345. [25 refs.]

The author and Professor ABRAMI, about eleven years ago, advanced the hypothesis that the malaria paroxysm was caused by a haemoclastic shock which preceded it by some hours. This paper reviews observations on the subject which have been made during the intervening years. In support of the hypothesis:—(*a*) The therapeutic action of induced malaria in general paralysis is similar to that of protein shock. (*b*) Examination of the blood at short intervals before the paroxysm shows that schizogony and leucopenia take place two or three hours before it occurs. (*c*) Certain manifestations, which are often associated with protein shock, such as urticaria and asthma, are sometimes associated with attacks of malaria. *W. F.*

GUYOMARC'H, TOULLEC & ALAIN. Episode démentiel et gangrène symétrique des extrémités au cours d'une infestation palustre à *Plasmodium praecox*. [**An Attack of Dementia with Symmetrical Gangrene, in a Case of Infection with** *P. falciparum*.]—*Bull. Soc. Path. Exot.* 1932. Apr. 13. Vol. 25. No. 4. pp. 307–310.

A young soldier was sent home from Morocco, very ill, wasted and anaemic; he suffered from delusions and lack of orientation. The

mental symptoms had appeared suddenly, three months before. On the day after admission to hospital, it was found that one in every four of his red cells contained a subtertian parasite. He was treated with quinine in large doses, by the mouth and into the gluteal muscles. The malaria and the mental symptoms disappeared at the same time, but he had no memory of the 3 months during which they had persisted. Family worries had been a predisposing cause. Four days after treatment was begun, the toes became blue and, eventually, gangrenous.

[The author attributes this to the malaria, and does not consider the quinine treatment as a possible cause.] *W. F.*

SCHULEMANN (W.). **Synthetic Anti-Malarial Preparations.**—*Proc. Roy. Soc. Med.* 1932. Apr. Vol. 25. No. 6. pp. 897–904 (Sect. of Trop. Dis. & Parasit. pp. 15–22). With 8 diagrams.

The author gives an outline of the experiments undertaken at the Bayer-Meister-Lucius Research Laboratories in the synthesis of anti-malarial preparations. The only drugs, other than quinine, which showed any definite action were methylene blue and salvarsan. The author and his colleagues based their experiments on methylene blue, and they put in new groups in place of those originally present in the molecule. The various products were tested by ROEHL on canaries infected with proteosoma.

" In one of the aromatic amino groups of methylene blue we substituted an aliphatic basic group in place of an alkyl radical. . . . We changed the position of the amino groups in the quinoline ring, introduced every conceivable substitute in the quinoline nucleus in addition to the amino group, and also used many other heterocyclic rings. Furthermore, we varied the side chains and finally the basic aliphatic group. . . . The length of the carbon chains was altered, and it was made into branched chains in many different ways. . . . The action of all these compounds was tested . . . by Roehl, and from among them we chose plasmoquine for practical clinical investigation."

Structual formulae are given, illustrating several of preparations which were tested on birds. The three types of malaria parasites react to drugs in different ways: arsenic compounds act on *P. vivax*, not on *P. falciparum*; methylene blue acts on *P. malariae*, but has little effect on *P. vivax* and none on *P. falciparum*; quinine does not produce the same effect upon all three species. Moreover, the various stages of development of the parasites react to drugs in different ways; for example, plasmoquine has no effect on subtertian schizonts but it destroys the gametocytes. Though treatment with plasmoquine will render a gametocyte-carrier incapable of infecting mosquitoes, Professor Schulemann considers that it will rarely be possible to treat every carrier in a district, and that, therefore, antimosquito measures are still necessary. MIETZSCH and MAUSS have elaborated a new compound (atebrin) which has been tested in animal experiments by KIKUTH in the Elberfeld Laboratories. It acts on the schizonts like quinine, and has no effect on the gametocytes; it also appears to reduce the number of relapses after treatment.

In the discussion following this paper Colonel S. P. JAMES said that, as Professor Schulemann had stated, the problem was fourfold: first, the problem of the sporozoites; second, that of the asexual parasites; third, that of the sexual forms; fourth, that of the forms responsible for relapses. Plasmoquine acted on the sporozoites, but was not entirely satisfactory because in an intensely malarious place it was

necessary to take more than 4 centigrams a day to secure protection, and that might produce toxic symptoms. Quinine and plasmoquine acted respectively upon the asexual and sexual stages, but no drug was yet known which acted upon the stage which was responsible for relapses. The chief difficulty in appraising the value of new remedies lay in the existence of many different strains of each species of malaria parasite, some of which were much more virulent, and resisted treatment more than others. *W. F.*

KIKUTH (Walter); SIOLI; PETER (F. M.). Zur Weiterentwicklung synthetisch dargestellter Malariamittel. [**Further Developments in Synthetically Produced Drugs for Malariatherapy, Atebrin.**] I. Ueber die chemotherapeutische Wirkung des Atebrin [KIKUTH].—*Deut. Med. Woch.* 1932. Apr. 1. Vol. 58. No. 14. pp. 530–531. [10 refs.]; II. Ueber die Wirkung des Atebrin bei der Impfmalaria der Paralytiker [SIOLI].—*Ibid.* pp. 531–533. With 5 text figs.; III. Ueber die Wirkung des Atebrin gegen natürliche Malariainfektion [PETER].—*Ibid.* pp. 533–535. With 1 text fig.

I. Chemotherapeutic Action of Atebrin.—The chemists, MIETZSCH and MAUSS, working in the research laboratory of the I. G. Farbenindustrie in Elberfeld, have developed the work on plasmoquine, and have made a new advance in malaria therapy by the production of the new drug Atebrin. Its constitutional formula will be published in the course of the present year. It is the dihydrochloride of an alkylaminoalkylaminoacridin derivative. The author has tested its chemotherapeutic properties experimentally, using for the purpose *Haemoproteus orizivorae,* present in the blood of finches. He established by his experiments that atebrin is a schizontocide, differing therefore from plasmoquine which is essentially a gametocide.

II. Action of Atebrin on Inoculation Malaria in G.P.I.—Sioli has shown that in inoculation malaria in cases of G.P.I. atebrin is a very active therapeutic agent, and has an unusual capacity for preventing relapses. He recommends 0·1 gm. thrice daily for several days. Single doses of 0·2 gm. and daily total doses of 0·6 gm. have been well tolerated; higher doses have caused gastrointestinal disturbance. Frequently a yellow colour of the skin is noted after administration of atebrin, this is temporary and has no ill effect on the health, it is due to a pigmentary action of the drug and not to jaundice.

III. Action of Atebrin in Natural Malarial Infection.—Peter treated cases of malaria in Rumania with atebrin, 3 cases of benign tertian (2 natural infection, 1 inoculated) and 2 cases of malignant tertian malaria. In the case of benign tertian the total dose of atebrin was 1 gm. and in the cases of malignant tertian 2 gm. Atebrin appears to be slowly excreted in the urine. He concludes, from the limited material, that atebrin acts on all stages of benign tertian parasite. It first destroys the rings, then the dividing forms and lastly it acts on the gametocytes. In the case of the parasite of malignant tertian malaria it rapidly destroys the rings, but is therapeutically inactive on the crescents; indeed he thinks the latter increase in the peripheral blood. He notes the yellow colouration of the skin. *E. D. W. Greig.*

MÜHLENS (P.). Die synthetischen Malariamittel Plasmochin und Atebrin. [**Synthetic Drugs, Plasmoquine and Atebrin, for Malaria-therapy.**]—*Muench. Med. Woch.* 1932. Apr. 1. Vol. 79. No. 14. pp. 537–540.

The author recalls that it was the shortage of quinine during the war which led to the production in Germany of plasmoquine, and he refers to its curative and prophylactic properties. He then goes on to discuss the new drug atebrin and refers to the work of KIKUTH, SIOLI and PETER (above). In Hamburg from 24th November 1930, to the end of February 1932, 122 cases (17 benign tertian, 8 quartan, 85 malignant tertian, 2 cases of quinine idiosyncracy and 10 post malarial conditions) were treated with atebrin alone and in combination with plasmoquine. His results confirm those of SIOLI and PETER. He finds that the rings in malignant tertian are more rapidly affected than by plasmoquine. Cases of quartan infection are also cured, but the gametocytes took longer to disappear than with plasmoquine. It was well tolerated by the subjects of quinine idiosyncracy and of blackwater fever. The author had also the opportunity of testing the drug during a journey in Mexico, Venezuela and Colombia from January to March 1931. On his return from S. America in April 1931 he continued his observations at Hamburg. From his various observations he concludes that (1) The 122 patients tolerated the drug well up to a total dose of 4·8 gm. In many cases a yellow discolouration of the skin developed during treatment, but without liver damage and it disappeared in 2 to 3 weeks at most. (2) Atebrin acts well on all three species of malarial parasite, but better on the schizonts than on the gametocytes. An ideal combination is with the gametocide, plasmoquine. (3) For malignant tertian a course of 7 to 10 days of atebrin, 0·1 gm. and plasmoquine, 0·01 gm., thrice daily is recommended. Whether or not after treatment will be required will have to be determined by further observations. (4) Atebrin is well tolerated in quinine idiosyncracy and blackwater fever. (5) Seeing that atebrin can be determined in the urine for weeks, exact observations on its prophylactic value are indicated. (6) Up to now the most promising medical prophylaxis is, 1 tablet daily of quinoplasmoquine or 2 tablets of plasmoquine co. (7) According to our observations the treatment of the three kinds of malarial infection with atebrin and plasmoquine gives at least as good results as with quinoplasmoquine. It is distinctly superior to simple quinine administration in its gametocidal action, even when quinine is given intramuscularly. *E. D. W. Greig.*

MÜHLENS (P.) & FISCHER (O.). Ueber Malariabehandlung mit Atebrin. [**Treatment of Malaria with Atebrin.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1932. Apr. Vol. 36. No. 4. pp. 196–207.

The essentials of this article will be found above. An interesting observation is recorded regarding the yellow colouration of the skin. They find that if patients taking atebrin are exposed to ultra violet radiation the yellow colour does not develop, but it is stated that the face becomes beautifully sunburnt in appearance without any hypersensitiveness to light as occurs in trypaflavine treatment. Also they noted that patients in the tropics who were exposed to the sun's rays for a time did not become yellow. They found that no damage was done to the system by the administration of atebrin; in particular

no disturbance of kidney function and of blood formation occurred. Interesting observations are being carried out on atebrin in urine by Dr. WEISE, which will be published later. *E. D. W. Greig.*

GREEN (Richard). **A Report on Fifty Cases of Malaria treated with Atebrin. A New Synthetic Drug.**—*Lancet.* 1932. Apr. 16. pp. 826–829.

Atebrin, originally called erion, is readily soluble in water, has a bitter taste and, like quinine, shows fluorescence in high dilution under ultraviolet radiation. It compares favourably with quinine in ridding the blood of malaria parasites, but it takes slightly longer to destroy subtertian rings and schizonts. It has no more effect upon crescents than quinine has, nor does it prevent their development in mosquitoes. It appears to be superior to quinine in preventing relapses ; 13 relapses were observed among 34 quinine-treated cases, but none among 19 treated with atebrin. A daily dose of 0·1 gram per 15 kilograms (33 lbs.) of body weight appeared to be the optimum. Two 0·1 gram tablets every morning, and one tablet every evening were given to the author's patients, with an average body weight of 48 kilograms (105 lbs.). The treatment was continued for seven days. The drug appears in the urine on the third or fourth day after the commencement of treatment, and can be detected for eight or nine days after it has been stopped. A rough test is the production of a characteristic yellow colour on adding acid to the urine and heating. The makers recommend extracting the alkalized urine with ether, and dissolving the residue resulting from the evaporation of the ether extract in strong sulphuric ; this assumes a yellow colour, strongly fluorescent. In about 14 per cent. of the cases a yellow discolouration of the skin and whites of the eyes was noticed ; this was an effect of the drug, not jaundice. This yellow colour generally appeared at the end of the course of treatment and lasted one or two weeks. Cases in which the drug does not appear in the urine by the third or fourth day of treatment are likely to become yellow. Four of the 50 patients complained of abdominal pain, severe in three cases, mild in one, intermittent and lasting some hours, occurring as early as the fifth day of treatment and as late as the fifth day after it had been stopped. Two patients complained of headache. An important difference from quinine is that atebrin appears to accumulate in the body. *W. F.*

NAPIER (L. Everard) & GUPTA (B. M. Das). **Atebrin : a Synthetic Drug for the Treatment of Malaria.**—*Indian Med. Gaz.* 1932. Apr. Vol. 67. No. 4. pp. 181–186. With 2 charts.

Eleven patients were each given one tablet containing 0·1 gram of atebrin, three times a day for four days. The fever was controlled and the asexual parasites disappeared from the peripheral blood, but crescents were not destroyed. There were no toxic symptoms or yellowing of the skin. The drug did not cause a reappearance of haemoglobinuria in a blackwater fever patient who was treated with it. A boy of 14 was given one tablet of atebrin, on the following day he was bitten by nine *A. stephensi* infected with *P. falciparum*, and he was then given one tablet daily for six days. Neither parasites nor fever appeared during the two months of subsequent observation, though

other persons bitten by the same batch of mosquitoes became infected. The authors conclude that atebrin had a prophylactic action in this instance. *W. F.*

ARBONA (Antonio). Ensayo preliminar con atebrina en el tratamiento de la malaria. [**Atebrin in Malaria.**]—*Bol. Asoc. Med. de Puerto Rico.* 1932. Vol. 24. No. 201. pp. 248–253.

The objects of the investigation here recorded were to determine the effect of atebrin on the temperature in malaria, the persistence of parasites after its use, the presence of toxic symptoms, if any, and finally the effects, when combined with plasmoquine, on the parasites and the patients. The daily dosage (divided into three doses) given for 5 successive days was 0·1 gm. atebrin and 0·01 [*i.e.*, 10] cgm. plasmoquine for children under 5 years, double this for those between 6 and 10 years, and treble for those of 11 years upwards [2 cgm. in place of 3 cgm. of plasmoquine is stated in some parts of the article; this may be a misprint.]

In a first series of 28 cases, 14 male, 14 female, 21 adults (*i.e.*, 11 years or over), 7 children, there were 19 with *P. vivax* infection (7 with gametocytes), 9 with *P. falciparum* (5 with gametocytes.) The temperature became normal in 1·4 days on an average in the benign tertian cases and 2 days in the subtertian. Only one patient, a lad of 16 years, still showed parasites in his blood after the course was completed.

In a second series of 23 patients, 11 over the age of 11 years, there were 18 females and 5 males, 12 with *P. falciparum* (3 with gametocytes), 11 *P. vivax* (4 with gametocytes). The average duration of the fever was 1·3 days, the temperature becoming normal in the *vivax* cases after 2·3 doses and the *falciparum* cases after 2·9. Two did not have the full course and disappeared; none of the remaining 21 showed any parasites after completion.

In the third series of 18, there were 11 "adults"; 16 had *P. falciparum* infection, and there was one each of *P. vivax* and *P. malariae*. The latter two were given atebrin alone, the others had the combined atebrin and plasmoquine. In 14 of the patients the blood was not negative for parasites till 4·1 days average, in 3 (all *falciparum* infections) they persisted till the sixth day, and in the other they were numerous after the seventh.

In his conclusions the author speaks highly of the combination since it leads to speedy control of the fever, rapid disappearance of the parasites from the peripheral blood and none of his patients showed any toxic symptoms. *H. H. S.*

THONNARD-NEUMANN (E.). Ueber Behandlung der natürlichen Malaria mit Atebrin in Columbien. [**Treatment of Malaria with Atebrin in Columbia.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1932. July. Vol. 36. No. 7. pp. 357–372.

At the suggestion of Prof. MÜHLENS the author treated 60 cases of malaria with atebrin alone or in combination with plasmoquine. Of the 60 cases, 49 were males and 10 were females, and one a child. The varieties of parasites were: 44 *P. falciparum*, 10 *P. vivax*, 6 a mixed infection of *P. falciparum* and *P. vivax*. The toxic effects noted after administration of the drugs were: yellow coloration of the skin of the white races; this disappeared in 2 weeks after cessation of treatment.

Abdominal pain, doubtless due to the plasmoquine, as it did not occur in cases treated with atebrin alone. The author concludes from his observations, which are fully set forth in tabular form, that atebrin is a powerful antimalarial drug and its clinical effects are excellent, even in cases of severe malignant tertian infection. The parasiticidal effect is especially on the ring forms. The action on the crescents in the doses given appears to be provocative. The combination of atebrin with plasmoquine caused in most cases a rapid disappearance of crescents. After 3½ months no relapses have been noted in his 60 cases. The doses employed were : atebrin 0·1 gm. in tablets thrice daily after food for 5 consecutive days. The tablet of atebrin and plasmoquine contained atebrin 0·1 gm., plasmoquine 0·01 gm., and was given in the same manner. *E. D. W. Greig.*

NAPIER (L. Everard), BUTCHER (Dorothy) & GUPTA (C. R. Das). **Field Experiments with Atebrin and Plasmochin.**—*Indian Med. Gaz.* 1932. Apr. Vol. 67. No. 4. pp. 186–191.

These observations were made at the Oxford Mission Settlement at Behala, where 50 out of 111 persons were found to be suffering from malaria. Plasmoquine was given in the very small dose of 0·01 gram, three times a week, to 46 persons. [The dose given by JAMES, this *Bulletin*, Vol. 28, p. 973, was 0·06 gm. daily for six days.] The result was the occurrence of more malaria among those taking prophylactic plasmoquine than among those who were not ; the drug, in these small doses, appeared to have a provocative effect. Thirty-five cases of malignant tertian and 13 of benign tertian were given a four-day course of atebrin, followed by a three-day course of plasmoquine. Five of the malignant, and two of the benign tertian cases relapsed during the next two months ; but re-infection could not be excluded. *W. F.*

DRENOWSKI (Angel K.). Therapeutische Versuche an Malariakranken mit Atebrin und Plasmochin. [**Therapeutic Tests with Atebrin and Plasmoquine in Malaria.**]—*Arch. f. Schiffs- u. Trop.-Hyg.* 1932. July. Vol. 36. No. 7. pp. 373–377. With 3 charts in text.

The author, who is the Director of the Malarial Institute in Burgas, Bulgaria, treated about 80 cases of malaria. He had accurate data for 57 which were divided into : malignant tertian, 6 ; benign tertian, 43 ; malignant and benign tertian, 8. After determination of the parasites in the blood each patient received 0·1 gm. atebrin combined with 0·01 gm. plasmoquine thrice daily for 6 days. The drugs were well tolerated, pain in the abdomen being occasionally complained of. The author noted that the combination of atebrin and plasmoquine, with very few exceptions, brought about a complete cessation of fever in 13 days. In order to produce complete destruction of gametocytes it is necessary to give after the completion of the 6-day course, a further course of plasmoquine alone, one tablet twice daily for 5 days. For the mass treatment of malaria in severely infected areas the combined treatment is preferable to treatment with quinine since the duration is shorter.

E. D. W. Greig.

STRICKLAND (C.) & ROY (D. N.). **The Behaviour of Plasmodia in the Mosquito after Treatment of the Human Host with Atebrin.**—*Indian Med. Gaz.* 1932. Apr. Vol. 67. No. 4. pp. 191–192.

Ten *A. stephensi* were fed on a patient during the last day of his four-day course of atebrin. Though his blood contained 200 crescents per cc., none of the mosquitoes became infected. Another batch was fed on the following day and, on this occasion, a few became infected. On the fourth day after the conclusion of treatment yet a third batch was fed, this time with full success. The authors conclude that atebrin prevents the development of gametocytes imbibed by a mosquito from a patient under treatment, and partly inhibits it on the day after treatment, but has no effect three days after treatment. (See GREEN above.) *W. F.*

PIEBENGA (P. J.). De malaria-epidemieen in het Geneeskundig Gesticht te Franeker en de gunstige invloed der chinoplasmine-behandeling. [**Malaria Epidemics in the Asylum at Franeker and the Satisfactory Effect of Quinine Plasmoquine Treatment.**]—*Nederl. Tijdschr. v. Geneesk.* 1932. Apr. 2. 76th Year. No. 14. pp. 1564–1578. With 3 figs. (1 on a double plate). English summary.

During the years 1928–1931 trial was made in Holland of different methods of treatment of malaria. These methods were the long and the short quinine and the combined quinine plasmoquine treatments. The long quinine treatment consisted of 1 gm. quinine sulphate for 14 days and then every 4 days for 3 months. In the short method the quinine was given for 7 days only: in the event of a relapse the treatment was repeated and finally after a fortnight 1 gm. quinine for 5 days as a prophylactic. The third method was by chinoplasmine tablets, one three times daily for 14 days. These tablets contain 300 mgm. quinine sulphate and 10 mgm. plasmoquine. Quite definite results were obtained. The long and the short quinine methods did not prevent relapses, whereas with chinoplasmine few or no relapses took place. A careful control of the administration of these tablets must be exercised, but except for this necessary precaution against toxic action the patient need not remain in bed. *W. F. Harvey.*

MANSON-BAHR (Philip). **The Therapeutic Effects of Plasmoquine in Pregnancy.**—*Lancet.* 1932. Apr. 23. pp. 882–883. [12 refs.]

The author has found the combination of quinine and plasmoquine well tolerated by pregnant women and unattended by danger to either mother or child in all three clinical varieties of malaria. He recommends a dose of "four tablets of the standardised product daily (0·04 gram of plasmoquine plus 0·5 gram of quinine sulphate) for 5 separate weeks with a pause of 3 days interval between each weekly course."

W. F.

MANWELL (Reginald D.). **Quinine and Plasmochin Therapy in *Plasmodium rouxi* Infections, with Further Notes on the Effects of these Drugs on the Other Avian Malarias.**—*Amer. Jl. Trop. Med.* 1932. Mar. Vol. 12. No. 2. pp. 123–147. [17 refs.]

Continuation of work recorded in this *Bulletin*, Vol. 28, p. 600.

"The work herein described has had for its object the solution of the problem as to whether the two species of avian plasmodia most refractory

to treatment could be more successfully treated with a combination of plasmochin and quinine, than with either drug used separately, and further investigation of the effect of plasmochin upon *Plasmodium elongatum*, shown in previous work to be very highly susceptible to plasmochin. *Plasmodium rouxi*, an Algerian species, has also been studied with reference to its chemotherapy and the results compared with those obtained by the same methods on the other three species. The question of the reliability of splenomegaly as an indication of malarial infection has also been investigated. A total of 120 cases have been treated, 44 have been used as controls, and 101 others have been used in testing for sterilization and in other ways. Allowing for duplications, 223 birds have been used. The following conclusions seem justified :—

" 1. Infections with *Plasmodium praecox* and *Plasmodium cathemerium* cannot be more successfully treated with a combination of plasmochin than with either drug separately, or at least such an advantage, if it exists, is slight. The results obtained in these researches gave no suggestion that such a superiority obtains.

" 2. Wide differences have been shown to exist in the susceptibility of different birds to treatment, when infected with *Plasmodium elongatum*, and these are interpreted as meaning that the effect of the drug used—plasmochin—is exerted indirectly, through a stimulation of some sort to the natural defensive powers of the host, as well as directly upon the parasite. In general, about four days of treatment appear to be necessary to prevent the development of the infection when started immediately after inoculation, and about twelve days appear to be required for sterilization when administration is deferred until parasites are evident in the blood.

" 3. Plasmochin exerts a direct plasmodicidal action, when parasites belonging to the species *elongatum* are exposed to the drug *in vitro*, but the action is slow and apparent only after a number of hours. Morphological changes are produced more quickly in the parasite than are changes in infectivity.

" 4. *Plasmodium elongatum* infections are less easily treated with plasmochin after they become chronic, but it is certain that the parasite level is forced down to a very low level—so low that the blood is no longer infective to clean birds—and that the level remains at this low point in most cases for at least two weeks, even though it is not fully demonstrated that sterilization occurred.

" 5. Infections with *Plasmodium rouxi* are as susceptible to plasmochin as are those of *elongatum*, and more susceptible to quinine than any of the other three species. Sterilized cases are as readily reinfected as when infected the first time.

" 6. The parasite-level establishes itself at a much higher point with chronic cases of *Plasmodium rouxi* than in chronic cases of any of the other three species studied.

" 7. Splenomegaly is not a trustworthy means of diagnosis in avian malaria, particularly chronic cases, since it may be absent, even when parasites are easily demonstrable in the blood, and is often present in birds dying from other causes and known to be, and to have always been, free from malaria. Even the colour of the spleen is not a reliable indication, unless it is very dark." *W. F.*

LEVENSON (E. D.). Contribution à l'étude de l'action de la plasmoquine sur la sécrétion du suc gastric. [**Action of Plasmoquine on Secretion of Gastric Juice.**]—*Trop. Med. & Vet.* Moscow. 1931 Vol. 9. No. 2. pp. 70–74. [In Russian. French summary p. 74.]

The author records experiments on the effect of plasmoquine on the secretion of gastric juice. Preliminary tests were made on *in vitro*

digestion of egg-white in Mett's capillaries in the presence of plasmoquine, which was found to have practically no effect upon the digestion of the protein by pepsin. Further experiments were conducted on human beings. The gastric juice was collected twice from each patient by means of a duodenal sound: once after a control "meal" consisting of 2 per cent. solution of methylene blue in 300 cc. of distilled water, the second time after a similar "meal" to which 0·02 gm. plasmoquine was added. In this manner sixteen persons were examined. It was found that in eleven cases there was an increase in the total acidity of the gastric juice, in seven there was an increase of free hydrochloric acid, and in six the digestive power of the gastric juice was augmented. On two occasions only was there a decrease in the digestive power of the juice. It is concluded that in most cases plasmoquine introduced *per os* stimulates the production of hydrochloric acid and the digestion of proteins. *C. A. Hoare.*

HENRY (Thomas Anderson). **The Standardisation of Mixtures of Cinchona Alkaloids.**—*Riv. di Malariologia.* 1931. Nov.-Dec. Vol. 10. No. 6. pp. 713–719.

The original quinetum consisted of the total alkaloids extracted from the red bark of *Cinchona succirubra*, which was the tree grown on the British Indian plantations. These trees yield but little quinine, and, in 1874, at the suggestion of Dr. J. E. de VRIJ, quinetum was prepared from their bark in factories attached to the government plantations, instead of sending it to Europe. However the *C. succirubra* trees were gradually displaced by other varieties yielding more quinine and, by 1887, the Indian factories were able to manufacture the sulphate. By 1903, so little red bark was grown that quinetum could no longer be prepared and, in its place, there was put on the market a mixture of the alkaloids of the new barks; in this case, however, not the total alkaloids, but those which remained after the quinine had been extracted. A certain amount of quinine was added to this mixture to make it approximately similar to the original quinetum, and it has since been known as cinchona febrifuge. It is made in India, Java, England and elsewhere; there is no recognized specification, its content of alkaloids varies within wide limits, and it therefore does not approach de Vrij's quinetum in quality and reliability. Some samples consist of artificial mixtures of the alkaloids in various proportions. In order to remedy this state of things, the Malaria Commission of the League of Nations has accepted the recommendations of a conference of pharmacological and chemical experts, held under its auspices at Geneva in May 1931, and reproduced in this *Bulletin* (*ante*, p. 461). *W. F.*

MANCA (S.). Il chineto nella cura della malaria. (**Quinetum in Treatment of Malaria.**)—*Riv. di Malariologia.* 1931. Nov.-Dec. Vol. 10. No. 6. pp. 720–742. [10 refs.] English summary (9 lines) p. 806.

This is an important article and only further trial can decide whether the claims made on the basis of so few cases can be sustained. The sub-committee of the League of Nations Malaria Commission has concluded that "the name 'Quinetum' should be reserved for a preparation consisting of quinine, cinchonidine and cinchonine in equal parts,

that being approximately the normal proportion of these alkaloids in Cinchona succirubra."

The author of this paper mentions two official [chineto di Stato] forms for oral administration: No. 1 containing, in percentages, 37 sulphate of quinine, 37 sulphate of cinchonidine, 25 sulphate of cinchonine; and No. 2 containing 29, 45·5, and 25 [52 is given in the text, but is obviously a mistake] per cent. and in either case "a limit of 5 per cent. of secondary alkaloids, quinidine, hydroquinine, cinchonine, etc." There is also a State preparation for subcutaneous injection put up in phials of 1 and 2 cc., containing 0·5 and 1 gm. of quinetum respectively [but which form is not specified].

The author describes in detail 22 cases, 7 of benign tertian infection, 10 of subtertian and 5 of both, stating in each case the condition of the blood, and the spleen and results during the courses of treatment and afterwards, the preparations used, their doses and the intervals between them. These facts can only be summarized here. Five patients (2 benign and 3 malignant tertian) were given the drug orally in doses (usually divided) of 1–2 gm. daily, for periods up to 32 days; the other seventeen were given injections, usually 1·5 gm., and occasionally 2 gm., in divided doses for 5 days, followed by oral administration, 1·5 gm. daily for a fortnight and thereafter 1 gm., the whole stay in hospital varying between 25 and 40 days. In practically all the fever came down promptly, parasites disappeared from the circulation within a week, the spleen rapidly decreased in size, the anaemia improved, in some to the extent of a million red cells per cmm. in a week or so. One gram was not sufficient either *per os* or *per cutim*, 1·5 was usually an adequate dose. Symptoms such as tinnitus, deafness, amblyopia and tremor, common after quinine, were evidenced only by slight tinnitus and tremor, neither of which caused any real trouble. Except in severe cases—pernicious malaria—1·5 to 2 gm. by mouth daily is recommended, the injections being reserved for the serious stages and followed after a few days by oral administration. None of the author's patients showed any idiosyncracy. *H. H. S.*

GROOTHOFF (A.). Quelques observations sur le problème du quinetum. [**The Problem of Quinetum.**]—*Riv. di Malariologia.* 1931. Nov.-Dec. Vol. 10. No. 6. pp. 703–712. English summary (8 lines) p. 806.

The author was formerly a director of the government cinchona plantations in the Dutch East Indies. He discusses the League's proposals with regard to Totaquina [*ante*, p. 461]. Many malarious countries contend that they are unable to provide sufficient quinine for their people because the price is too high. This is why the Health Section of the League of Nations has interested itself in quinetum and totaquina, and why it hopes to increase the amount available, by extending the planting of cinchona, especially those varieties rich in total alkaloids. The author discusses the economic aspects of this proposal and begins by outlining the history of cinchona cultivation, and its salvation by the quinine convention (see de VOGEL above). At present 95 per cent. of cinchona producers are affiliated to the Kina Bureau which is established at Amsterdam and is composed of representatives of the planters and the manufacturers. The present price is 37·50 florins for a kilogram of quinine sulphate; of this the planter receives 18, and the manufacturer 19·50. The author thinks that 25

florins would be a fair price. The Dutch Indies produce 10,000,000 kilograms of bark, the British Indies 850,000, and other countries 250,000. The Dutch Indies can provide from their bark 630,072 kilograms of quinine sulphate, and 161,893 of quinetum containing 19·7 per cent. of quinine. The rest of the world can supply 93·830 kilograms of quinetum. The total world supply is therefore 630,672 of quinine and 255,723 of quinetum. If one wishes to increase the supply of quinetum by 100,000 kilograms, it will be necessary to bring 1,465 hectares of plantations into bearing, which will require much capital and careful selection of soil. Moreover the plantations of Java have only been kept going by regulating the supply to the demand; this demand has not increased during recent years, and some plantations have gone out of cultivation. It does not seem good business to plant up fresh areas elsewhere; a great slump in prices has always meant a great decrease in output and, later on, high prices; consequently such a policy will not help malarious countries. Moderate prices and an assured market mean a steady supply. *W. F.*

St. John (J. H.). **Quinine Analysis of the Blood with Reference to the Treatment of Malaria.**—*Amer. Jl. Trop. Med.* 1932. Mar. Vol. 12. No. 2. pp. 101–116. With 7 text figs.

Some people do not develop and maintain such high concentrations of quinine in their blood as others. This may explain why some people are harder to cure than others. Continued administration in the same doses does not necessarily result in increased concentration of quinine after the first 24 hours. If 1·950 grams (30 grains) are given by the mouth in capsules, the maximum concentration of about 6 mgm. per litre of blood is reached in approximately 1 hour, and is maintained for about 8 hours. With smaller doses it takes longer to reach this concentration. A dose of 650 mgm. (10 grains) every 8 hours, produced a concentration of 6 mgm. per litre, 1 hour after the second dose, and then maintained it. A dose of 5 grains every four hours produced the same concentration, but it took 24 hours, or four doses, to do so. The maximum once reached could be maintained by this small dose as long as desired. The highest concentration was obtained by 10 grains every four hours, and was above 10 mgm. per litre in most cases; this can be maintained for 4 or 5 days. High concentration can be reached more speedily by giving the first three doses at two-hourly intervals. *W. F.*

Alessandro (Antonio). L'adrenalina nella cura della splenomegalia malarica cronica. [**Adrenalin in Malarial Splenomegaly.**]—*Riv. Sanitaria Siciliana.* 1932. Mar. 1. Vol. 20. No. 5. pp. 332, 335–338, 341–342. English summary (6 lines).

The author administered adrenalin intravenously to 7 patients with splenomegaly due to chronic malaria, starting with 1/100 mgm., then proceeding with 1/80, 1/70 and so on to 1/20 or, if tolerated, to 1/10 mgm.—some 2–3 mgm. being given altogether. He noted the effects on the splenic enlargement, on the haemopoiesis, and on the general state. He gives details of each of the 7 cases; in 3 the spleen reached to the level of the umbilicus and in none was it less than 3 fingers' breadths below the costal margin. In four (one of whom had a spleen to the umbilical level) the spleen returned to normal; in all it was much reduced. The red corpuscles which before treatment were 2·5 to 3

million per cmm. increased by a maximum of 2,100,000 and a minimum of 800,000, and the leucocytes by 300 to 1,800 ; haemoglobin increased by 8 to 30 per cent. The weight increased by 1·9 kgm. in the least to 7·1 kgm. in the greatest. The number of injections varied from 30 in 45 days to as many as 55 in 12–13 weeks. All the patients showed improved appetite and stated that they " felt much better." [No mention is made of any treatment other than the adrenalin injections.]

H. H. S.

LOTZE (Harald). Die künstliche Proteosomainfektion der Vögel. 3. Mitteilung. Ein Beitrag zur Frage der Therapie bei Vogelmalaria. [**Therapy of Bird Malaria.**]—*Zent. f. Bakt.* I. Abt. Orig. 1932. Mar. 30. Vol. 124. No. 3/4. pp. 161–167. With 5 charts in text.

A series of birds infected with proteosoma received from the 2nd to the 6th day of the infection the following forms of treatment :—(1) 0·1 cc. blood taken from the wing vein and immediately injected into the same bird subcutaneously (autohaemotherapy). (2) 0·1 cc. blood taken from another infected bird and injected intramuscularly. (3) 0·05 cc. serum, obtained from blood taken at the height of infection from a bird that had been killed, injected intramuscularly. (4) 0·1 cc. of a suspension of blood corpuscles in normal saline, made from blood taken at height of infection from a bird that had been killed, injected intramuscularly. Charts illustrate the course of the experiments. He concludes that :—The treatment of bird malaria by autohaemotherapy is, on technical grounds, unworkable. Results of treatment were better with fresh serum of infected animals and a suspension of infected blood cells in normal saline ; in the latter therapy there was complete disappearance of the parasites from the tissues of the animals. Reports of similar therapeutic procedures in human malaria appear to support the results of the experiments. *E. D. W. Greig.*

i. TRENSZ (F.). Essai d'application de la réaction de Henry à l'étude épidémiologique du paludisme. [**Henry's Reaction in the Study of Malarial Epidemiology.**]—*Bull. Soc. Path. Exot.* 1932. Apr. 13. Vol. 25. No. 4. pp. 310–314. With 1 chart in text.

ii. ——. La réaction de Henry (" séroflocculation palustre ") et la " surfloculance " de certains sérums de paludéens. [**Henry's Reaction. Superflocculance with Certain Malarial Sera.**]—*Ibid.* pp. 314–317.

i. The instability of the blood proteins shown by Henry's reaction does not depend upon the intensity of infection. When the reaction was tested in a native village, it was found that there were fewer positives in the malaria season than before it, and that there were fewer positives in children than in adults, though malaria tends to cure itself with age, The splenic index must remain the method of choice in an epidemiological survey.

ii. Sometimes the control tubes in Henry's reaction (which contain serum and distilled water, without antigen) show a flocculation, which Henry calls " surflocculance." Such superflocculance occurs especially with sera giving a positive reaction in the tubes of test which contain serum, antigen, and salt-solution ; the stronger the positive reaction, the greater the superflocculance. If a guineapig is inoculated with

trypanosomes its serum gives a positive Henry's reaction soon after the appearance of the parasites in its blood. As the infection advances the reaction becomes more intense, and eventually flocculation occurs in the control tubes without any antigen. The author concludes that the two reactions, namely that with the antigen and that without it, are both due to the same change in the serum, and that the difference is only one in degree. Marcel LEGER remarked, in the discussion following the first paper, that as the author had shown that a positive reaction followed infection with a protozoon (trypanosome) which produced no pigment, Henry's melanin could no longer be regarded as a specific antigen. *W. F.*

TRENSZ (F.). Le rôle du pH des réactifs dans la sérofloculation du paludisme (réaction de Henry). [**The pH of the Reagents in Henry's Reaction.**]—*Bull. Soc. Path. Exot.* 1932. Mar. 9. Vol. 25. No. 3. pp. 221–224. With 1 text fig.

This presents no difficulties, since the reaction takes place over the wide range of pH 5.4 to pH 9.0. The optimum appears to be that which coincides with a minimal molecular concentration, that is to say, pH 7 of distilled water. *W. F.*

LIVIERATO (S.), VAGLIANO (M.) & CONSTANTAKATO (G.). Utilisation d'un nouvel antigène pour le diagnostic de la malaria par la méthode de floculation. [**A New Antigen for the Flocculation Test in Malaria.**]—*C.R. Soc. Biol.* 1932. May 13. Vol. 110. No. 16. pp. 26-27.

In place of Henry's antigen which is made from the pigment of an ox's eye, the authors have prepared one from the sac of a cuttlefish with equally good results. *W. F.*

ELLER (Karl). Serologische Untersuchungen bei Tertiana-Impfmalaria an luesfreien Patienten. [**Serological Investigations on Inoculation Malaria in Non-Syphilitic Patients.**]—*Ztschr. f. Immunitätsf. u. Experim. Therap.* 1932. Vol. 74. No. 3/4. pp. 397–420.

As a result of his investigations the author reaches the following conclusions :—(1) Serological investigations with the usual methods and technique for the diagnosis of syphilis give positive results in malaria in persons not suffering from syphilis and the reactions cannot be distinguished from the positive reactions of syphilis. This applies to infection both by mosquitoes and inoculation. (2) By the use of the Meinicke turbidity reaction, however, the results are different. It appears that the reaction products in the serum of patients suffering from syphilis and malaria show quantitative and qualitative differences. In malaria they are not identical with immune bodies as in syphilis. (3) He considers the further pursuit of this study will be of interest clinically for differential diagnosis of malaria and syphilis not only in the tropics, but in the use of malarial therapy, and also for the elucidation of the nature of serological reactions. *E. D. W. Greig.*

TSECHNOWITZER (M. M.) & MOLDAWSKAYA-KRITSCHEWSKAYA (W. D.). **The Intracutaneous Test in Malaria.**—*Trop. Med. & Vet.* Moscow. 1931. Vol. 9. No. 6. pp. 261–264. [In Russian. English summary.]

Having failed in their attempts to obtain a skin reaction with antigens contained in the plasma and serum of malarious patients, the authors prepared an antigen derived from the plasmodia and the products of their metabolism contained in the red cells. 5 cc. of blood, taken from the vein during an attack and containing 10–15 parasites per field in a thick film, are diluted in 250 cc. distilled water. The mixture is thoroughly shaken and left for 24 hours at room temperature. The fluid part of the mixture is then removed, the sediment is poured into sterile 40–50 cc. test-tubes and centrifuged. The supernatant fluid is decanted and the sediment repeatedly washed until the fluid is colourless. The sediment is then made up to its original volume with distilled water, the resulting mixture representing the stock solution of antigen. It is warmed in a water bath to 56°C. and 0·25 per cent. carbolic acid is added to it. After diluting the solution by 32, 64 and 128 volumes it was used for the reaction, 0·1 cc. being injected intracutaneously. To this antigen the name " malaren " was given.

Another antigen, named " haemo-antigen " or " haemomalaren," was prepared according to HERMAN and LIFSHÜTZ (*Kazan Med. J.* 1929, No. 12) : malarial blood was diluted with distilled water, 1 : 50, and boiled ; 0·5 per cent. carbolic acid was then added to the cooled mixture. 0·1 cc. of this antigen was employed for the skin reaction in dilutions of 1 : 5,000 and 1 : 10,000. The authors also employed a mixture of the two antigens (" complex " antigen) in their respective doses. Blood containing *Plasmodium vivax* and *P. falciparum* was used. Analogous preparations from the blood of healthy subjects were used as controls.

The intracutaneous injection was made on the inner-surface of the arm. After the administration of the antigen a swelling (bulla) 7·8 mm. in diameter, appears at the site of injection. The skin reaction was estimated twice : after 24 and 48 hours. In positive cases there is a hyperaemia extending over an area from 8 to 50 mm. in diameter, sometimes accompanied by haemorrhages 8–12 mm. in diameter. In negative cases there is no reaction at the site of injection.

The test was applied to 85 cases of malaria and to 49 control subjects. The reaction was positive in 92·7 per cent. of cases with parasites in the blood, in 88 per cent. of chronic cases, in 53·9 per cent. of cases with a history of malaria in the past, and 15·5 per cent. in controls. The best results were obtained with the " complex antigen." The reaction is not specific to the different forms of malaria. *C. A. Hoare.*

DE LANGEN (C. D.). Polynucleaire leukocyten bij de phagocytose van malariaparasieten. [**Polynuclear Leucocytes concerned in the Phagocytosis of Malaria Parasites.**]—*Geneesk. Tijdschr. v. Nederl. Indië.* 1932. June 7. Vol. 72. No. 12. pp. 793–794. With 2 figs. on 1 plate.

In two cases of subtertian the author noticed phagocytosis of the merozoites by young polynuclear leucocytes. Whether this occurs regularly in certain stages of the attack or only in cases in which the parasites are very numerous is undecided. Hitherto only monocytes were known to take part in the phagocytosis of the parasites.

The author's staining method is the following :—

A drop of blood is taken from the finger tip, which is previously covered with a drop of 1 per cent. brilliant kresyl blue, pH 7. The drop is immediately mixed with the stain and left for two minutes. Then an ordinary blood film is made from the mixture which after fixation by methyl alcohol is stained again with Giemsa solution.

The photograph looks convincing. *W. J. Bais.*

KONSTANSOW (S. W.). [**The Nature of Schüffner's Dots in Red Cells in Malaria.**]—*Trop. Med. & Vet.* Moscow. 1931. Vol. 9. No. 6. pp. 264–267. [In Russian.]

The author states that Schüffner's dots can be invariably produced by addition of 0·02–0·04 per cent. sodium carbonate to the ordinary Giemsa solution with which the blood film containing *Plasmodium vivax* is stained. He believes that the stippling is brought about by a change in the dispersion of the colloidal solution of the stain, resulting in the precipitation of the liquid dispersed phase in the form of drops. The phenomenon is caused by the introduction of the electrolyte (Na_2CO_3). To explain why the phenomenon is produced only in *P. vivax*, the author supposes that the products of metabolism of the latter have the same coagulating effect as the sodium salt.

C. A. Hoare.

WATS (R. C.) & WHITE (W. I.). **The Malarial Pigment (Haemozoin) in the Spleen.**—*Indian Jl. Med. Res.* 1932. Jan. Vol. 19. No. 3. pp. 945–950.

Paraffin sections containing malarial pigment were treated with xylol to remove the paraffin, alcohol to remove the xylol, and water to remove the alcohol ; they were then subjected to the action of various chemicals and the action on the pigment was noted. The pigment was not dissolved by acids or acid alcohol, nor by fat-solvents such as ether and chloroform ; it was bleached by hydrogen peroxide. It was completely dissolved by alkalis such as normal soda. It became brown when the alkali was first poured on ; and turned red if acid were substituted for the alkali before solution took place. The authors regard this as a specific test for haemozoin in the tissues. *W. F.*

GREEN (Richard). **Notes on the Use of Thick Blood Films in the Diagnosis of Malaria.**—*Bull. Inst. Med. Res. Federated Malay States.* 1931. No. 1. 10 pp.

Dry the thick film in an incubator for 2 hours, or at room temperature for at least 8 hours. Stain film before it is 24 hours old. The solutions required are :—

(*a*)

Azur II-Eosin	3·0 gram.
Azur II	0·8 ,,
Glycerine (pure)	250 cc.
Methyl Alcohol	250 cc.

Or, alternatively, one Soloid (B.W.) Eosin-Azur ground up, and dissolved in 5 cc. of equal parts of glycerine and methyl alcohol.

(*b*)

Buffered solution consisting of :—

Potassium dihydrogen phosphate	...	1 gram.
Disodium monohydrogen phosphate	...	2 ,,
Water	...	1 litre

The slides are placed on their edges in a staining trough. The stain is prepared by mixing the two solutions in the proportion of one drop of (*a*) to three drops of (*b*). Sufficient is prepared to fill the trough until the slides are immersed. Stain for one hour ; remove and dip gently in tap water five or six times. Tilt slides almost vertically to dry. Use no blotting paper.

[Copies of full instructions can be obtained from the Institute for Medical Research, Kuala Lumpur, F.M.S.] *W. F.*

NAPIER (L. Everard), KRISHNAN (K. V.) & LAL (Jemadar Chiranji). **Cytological Studies of the Blood and Tissues in Kala-Azar and Associated Conditions. Part III. Large Mononuclear Cells in Human Malaria.**—*Indian Med. Gaz.* 1932. Mar. Vol. 67. No. 3. pp. 135–139. With 2 charts in text. [10 refs.]

The blood cells were stained by a method of supravital staining ; details of this method will be published later. An excellent coloured plate is given, and also a table comparing the different characteristics of lymphocytes, monocytes, and histiocytes. One of the beneficial functions of antimalarial drugs (quinine, plasmoquine, and atebrin) appears to be the production of an increase of both the monocytes and the histiocytes, and a stimulation of their phagocytic activity. *W. F.*

SOESILO (R.) & VAN DER HOUT (O. H.). Het verband tusschen melasse-liquidatie in irrigatie-leidingen en malaria ; de ecologie van *Anopheles aconitus*. [**The Connexion between the Liquidation of Molasses into Irrigation Canals and Malaria ; the Ecology of** *Anopheles aconitus*.]—*Geneesk. Tijdschr. v. Nederl.-Indië.* 1932. June 21. Vol. 72. No. 13. pp. 842–850. [10 refs.]

The depreciation of molasses caused the sugar factories of East Java to get rid of it, the easiest way being to sluice it into irrigation canals. The common malaria carrying mosquito of East Java is *A. aconitus*. The larvae of this as well as of other species of Anophelines were found in much smaller numbers in irrigation water containing 1 : 1,000 molasses than in samples from the vicinity containing no molasses. The water, usually alkaline (pH 8·3), is rendered acid (pH $<$ 7) by the addition of the molasses. In accordance with other observations the authors found that aconitus larvae prefer water with little organic matter and proteid NH_3.

From an hygienic as well as from an agricultural point of view the addition of molasses to the irrigation water of the rice fields appears to be a favourable factor. *W. J. Bais.*

EJERSITO (Antonio) & LAUREL (Alberto G.). **Report on the Malaria Survey of the Proposed Negative Barrio at Malaking Patag (Cogonal Grande), Culion Island.**—*Monthly Bull. Philippine Health Serv.* 1931. Sept. Vol. 11. No. 9. pp. 467–479. With 1 map & 2 figs. on 1 plate.

" Anopheles larva density cannot and must not be held as criterion for the adult density thereof. . . . *A. funestus* larvae were rated only as 9 per cent. against 91 per cent. *A. barbirostris* larvae, *A. funestus* adults were 95 per cent. as against 5 per cent. *A. barbirostris* adults." *W. F.*

SAMBON (M.). Les index malarien, gamétien et splénique chez l'indigène adulte. [**The Parasite, Gametocyte and Splenic Indices in Adults.**]—*Ann. Soc. Belge de Méd. Trop.* 1932. June 30. Vol. 12. No. 2. pp. 241–244.

The parasite index of adults at Panda was 73, the gametocyte index was 3, the splenic index was 15·7. *W. F.*

MOUFEL (P.). [**Bibliography of Russian Works on Malaria.**]—*Trop. Med. & Vet.* Moscow. 1931. Vol. 9. No. 10. pp. 506–526. [In Russian.]

A list of 1,049 Russian publications on malaria, in continuation of those previously noted in *Trop. Dis. Bull.* *C. A. Hoare.*

ALESSANDRINI (Mario). Relazione su alcuni casi di malaria primitiva autoctona nel comune di Ancona. (On Some Cases of Primary Autochthonous Malaria in Ancona.)—*Riv. di Malariologia.* 1932. Jan.-Feb. Vol. 11. No. 1. pp. 30–34. English summary p. 133.

AUBERTIN (Charles). Paludisme et leucémie myéloïde.—*Bull. et Mém. Soc. Méd. Hôpit. de Paris.* 1932. Mar. 28. 48th Year. 3rd Ser. No. 11. pp. 435–438.

BABLET (J.). A propos d'un cas d'accès pernicieux palustre à forme pseudo-béribérique.—*Arch. Insts. Pasteur d'Indochine.* 1931. Apr. No. 13. pp. 73–80. With 1 chart in text & 4 coloured figs. on 2 plates.

BOYD (J. E. M.). Malaria in India.—*Jl. Roy. Army Med. Corps.* 1932. Feb., Mar. & Apr. Vol. 58. Nos. 2, 3 & 4. pp. 81–91; 177–194; 248–261. [24 refs.]

BURKE (G. T.). A Case of Malaria with Cerebellar Localization.—*Indian Med. Gaz.* 1932. Apr. Vol. 67. No. 4. pp. 197–198.

CAWSTON (F. G.). The Present Problem of Malaria in Natal.—*Jl. Trop. Med. & Hyg.* 1932. June 15. Vol. 35. No. 12. p. 185.

CIUCA (M.). Work of the Malaria Commission of the League of Nations.—*Chinese Med. Jl.* 1932. Apr. Vol. 46. No. 4. pp. 412–424.

COLOMBO (U.). La prophylaxie individuelle antimalarienne parmi la population europeenne d'Elisabethville (Katanga).—*Ann. Soc. Belge de Méd. Trop.* 1932. Dec. 31. Vol. 11. No. 4. pp. 373–385.

COULON (G.) & SAUTET (J.). Les rechutes à longue échéance dans le paludisme.—*C. R. Soc. Biol.* 1932. May 6. Vol. 109. No. 15. pp. 1322–1326.

DUCOSTÉ (Maurice). L'impaludation cérébrale.—*Bull. Acad. Méd.* 1932. Apr. 12. 96th Year. 3rd Ser. Vol. 107. No. 14. pp. 519–524.

EGYPTIAN GOVERNMENT. Anti-Malaria Commission. Report No. 6 of the Anti-Malaria Commission for the Fiscal Year 1929–1930. The Work of the Anti-Malaria Commission in combating Malaria in Egypt.—12 pp. 1932. Cairo: Govt. Press. [P.T. 20.]

FARINAUD (E), TOUMANOFF (C.) & HOANG-THUY-BA. Le paludisme à Tuyên-quang. Enquête malariologique.—*Bull. Soc. Méd.-Chirurg. Indochine.* 1932. Jan. Vol. 10. No. 1. pp. 66–87. With 1 chart & 1 folding plan.

HIYEDA (K.). Malaria in Manchuria.—*Jl. Oriental Med.* 1932. Mar. Vol. 16. No. 3. [In Japanese. English summary p. 36.]

HUDSON (E. H.). Sur le paludisme en Proche Orient.—*Bruxelles-Méd.* 1932. May 8. Vol. 12. No. 28. pp. 763–769. With 1 map in text.

KAMISAWA (Osamu) & ISHIOKA (Hiozo). Studies in the Treatment of Malaria. VI. Therapeutic Effects of Quinine administered intravenously against Malaria.—*Taiwan Igakkai Zasshi (Jl. Med. Assoc. Formosa).* 1932. Apr. Vol. 31. No. 4 (325). [In Japanese. English summary p. 37.]

KINGSBURY (A. Neave) & AMIES (C. Russell). The Attempted Control of Malaria by Plasmoquine Prophylaxis.—*Bull. Inst. Med. Res. Federated Malay States.* 1931. No. 3. 25 pp. With 8 figs.

KONSTANSOFF (S. W.). Zur Frage nach der Herkunft und der Natur [illegible] Schüffner Tüpf[illegible] Orig. 1932. [illegible] pp. [illegible]

KUMM (Henry W.). Observations on Two Malaria Vectors [illegible] Records of Other *Anopheles* in the States of Bahia and Sergipe, Brazil.—*Ann. Trop. Med. & Parasit.* 1932. [illegible] With 1 map.

LÉGER (J. P.). Un aspect de l'endémie palustre en Emyrne.—*Bull. Soc. Path. Exot.* 1932. [illegible] 10. [illegible] fig.

LEGER (Marcel). [illegible] la Guadeloupe.—*Bull. Soc. Path. Exot.* 1932. Mar. 9. [illegible] pp. 211–215.

DE MELLO (Froilano), in collaboration with VERNENCAR (Roguvira Sridora Poi). Sur la valeur des diverses méthodes de mensurations spléniques pour le dressage de cartes malariennes. Reprinted from *C. R. 2e Congrès International du Paludisme, Alger, 1930.* Vol. 1. pp. 527–548. With 2 text figs. & 9 graphs.

MONIER (H. M.). Renseignements recueillis sur le paludisme à Thakhek (Laos) au cours d'une visite effectuée en février 1932.—*Bull. Soc. Path. Exot.* 1932. May 11. Vol. 25. No. 5. pp. 419–421.

MORIN (Henry G. S.). Vers la prophylaxie sociale du paludisme.—*Bull. Soc. Méd.-Chirurg. Indochine.* 1932. Jan. Vol. 10. No. 1. pp. 88–128. With 1 fig.

PECORI (G.) & ESCALAR (G.). La lutte contre le paludisme dans la Campagne Romaine en 1930.—*Bull. Office Internat. d'Hyg. Publique.* 1932. Feb. Vol. 24. No. 2. pp. 274–277.

SCHACHSUWARLY (M.). Die Behandlung der Malaria mit Plasmochin.—*Arch. f. Schiffs- u. Trop.-Hyg.* 1932. July. Vol. 36. No. 7. pp. 378–384. [24 refs.]

SMITH (E. C.). A Case of Malaria with a Blood Picture Suggestive of Splenic Anaemia.—*West African Med. Jl.* 1932. Apr. Vol. 5. No. 4. pp. 69–70. With 3 figs. (1 coloured) on 2 plates.

SPENCER (H. A.). Pulmonary Conditions associated with Malaria Bronchomycoses.—*Jl. Trop. Med. & Hyg.* 1931. Apr. 15. Vol. 34. No. 8. pp. 106–108.

TORRIOLI (Mario). Su di un caso di porpora malarica. (On a Case of Malarial Purpura.)—*Riv. di Malariologia.* 1932. Jan.-Feb. Vol. 11. No. 1. pp. 35–41. With 1 chart. English summary p. 134.

TOUMANOFF (C.). Sur la présence d'une variété d'*Anopheles jeyporiensis* James au Tonkin et son rôle dans la transmission locale du paludisme.—*Bull. Soc. Path. Exot.* 1931. Dec. 9. Vol. 24. No. 10. pp. 958–967. With 8 text figs. [Refs. in footnotes.]

TRABAUD (J.). Les fugues palustres.—*Rev. Prat. Malad. des Pays Chauds.* 1931. Dec. 10th Year. Vol. 11. No. 12. pp. 555–556.

VAN DEN BRANDEN (F.). La plasmochine, dérivé synthétique de la quinoléine dans le traitement du paludisme.—*Bruxelles-Méd.* 1932. May 22. Vol. 12. No. 30. pp. 825–830.

VYAS (B. N.) & BHATIA (B. B.). On the Failure of *Toddalia aculeata* in the Treatment of Malaria.—*Indian Med. Gaz.* 1932. Apr. Vol. 67. No. 4. pp. 192–194.

YAWS AND SYPHILIS.

RAMSAY (G. W. St. C.). **Yaws and Syphilis in Calabar, Southern Nigeria : an Analysis of 5,000 Sachs-Georgi Tests.**—*Ann. Trop. Med. & Parasit.* 1932. July 14. Vol. 26. No. 2. pp. 149–155. With 2 graphs.

2,600 children between the ages of 4 and 16 years and 2,400 adults, from schools and out-patient departments, Calabar, were examined by Sachs-Georgi test. The incidence of positive reactions in children was 32–42 per cent. with a maximum at 6 years of age.

The author then says, " among children of sixteen years of age and under, acquired syphilis is most unlikely to occur " and thus believes the incidence of positive reactions is an indication of the incidence of yaws [a statement which is quite unwarranted unless he has *proved* that syphilis does not occur among the child population he is dealing with. Infantile acquired syphilis is very common among some native communities.]

The figure for adults rises gradually from 32 per cent. at 16 years to 50 per cent. at 40 years—due the author suggests, but without proof, to the combined effects of syphilis and yaws reinfections. [The figures adduced prove nothing beyond the fact that yaws and/or syphilis are common diseases.] *H. S. Stannus.*

TAKASAKI (S.). Zur Klinik der Frambösie im Kindesalter. [**Clinical Manifestations of Yaws in Children.**]—*Jahrb. f. Kinderheilk.* 1932. Jan. Vol. 134 (3rd Ser. Vol. 84). Nos. 3/4. pp. 169–181. With 23 figs.

A general account of the clinical manifestations of yaws in children as seen by the author during the years 1919–29 spent in the islands of Truk and Palau, Caroline Is., containing no new facts. A few points need notice. Emphasis is laid upon the insignificance of the initial lesions in some cases so that they pass unnoticed, also upon the fact that the patient rarely presents himself in the primary stage. The author in 10 years saw only 12 primary lesions. Though, he says, lesions on mucous membranes are denied by some observers yet he has established their occurrence ; he has also seen parenchymatous conjunctivitis, keratitis and iritis in yaws. [Mucous membrane lesions should be received with scepticism ; it is not generally realized that a lesion may " creep " over a muco-cutaneous junction or go further with healing in the skin area giving the appearance of a lesion of the mucous membrane in truth, but not one originating in the mucous membrane. The same is probably true of the conjunctivitis-iritis.]

H. S. S.

FITZGERALD (G. H.) & DEY (Nepal Chandra). **Unusual Types of Primary Lesions in Yaws.**—*Indian Med. Gaz.* 1932. Feb. Vol. 67. No. 2. p. 82. With 1 text fig.

The authors record three cases of primary yaw which they believe to exemplify two rare forms of initial lesion—(*a*) a punched out non-indurated, non-adherent ulcer of skin, resembling a gumma, (*b*) a large heaped-up lesion formed of crust-covered granulations between 2 and 3 inches in diameter.

[These three cases occurred in a series of 700 cases of yaws but the authors add that there were only 29 cases of primary or secondary eruption. It would therefore appear that they are not necessarily rare lesions.] *H. S. S*

SCHÖBL (Otto) & HASSELMANN (C. M.). Ueber Beziehungen zwischen Framboesie und Syphilis. [**Relations between Syphilis and Yaws.**] —*Beihefte z. Arch. f. Schiffs- u. Trop.-Hyg.* 1932. Vol. 36. No. 2. pp. 1–36 (105–140). With 8 text figs.

In this paper the authors traverse the ground already covered by SCHÖBL's articles in the *Philippine Journal of Science* reviewed in this *Bulletin*. Some of the points he makes may be restated as the matter is of considerable interest. Morphologically, culturally and by methods of staining, the treponemata of yaws and syphilis cannot be differentiated but they may be separated on the ground of their different biological behaviour in the body tissues. The organism of yaws is ectodermotropic and finds its home in the outer layers of the skin while *T. pallidum* is mesodermotropic and attacks all the organs of the body but prefers mesodermic tissues. This difference in tropism explains the different pathology in the two infections and immunity reactions, the differences in epidemiology and clinical manifestations, as well as inheritance in syphilis and not in yaws.

The immunity in these treponematoses is a real immunity which according to its degree limits the multiplication of the parasites or suppresses them altogether. With the development of a high grade homologous immunity in either there is also a heterologous immunity to the other. Heterologous immunity develops later than homologous immunity, immunity showing itself by a lengthening of the incubation period and change in the reaction capacity of the tissues to subsequent attempted reinoculation. When complete immunity is established further progress in the disease is prevented ; reinoculation and superinoculation fail. Resistance to infection is not due to a so-called latent infection. Immunity may be produced by inoculation with dead treponemata as antigens and they have reciprocal actions. Syphilis and yaws may be present together in the same case ; the immunity resulting mutually affects the course of each disease.

The possibility of exciting immunity in early cases of treponematous disease by means of killed vaccines and thereby preventing the later manifestations of the disease and its relationship to chemotherapy need full consideration. *H. S. S.*

TURNER (Thomas B.) & CHAMBERS (J. H.). **Experimental Yaws. I. Comparison of the Availability of the Rabbit and Monkey for the Isolation of Strains of Yaws.**—*Bull. Johns Hopkins Hosp.* 1932. Apr. Vol. 50. No. 4. pp. 253–269. With 4 figs. [11 refs.]

The authors propose to carry out investigations " designed to throw light upon the question whether or not yaws and syphilis are identical diseases," and " whether there is any immunological relationship between strains of spirochaetes recovered from yaws patients, on the one hand and from syphilitic patients on the other " both " *recovered in the same locality* " (Haiti). For yaws, monkeys (*Macacus rhesus*) when used were inoculated over each eyebrow by scarification and intracutaneously over each deltoid ; rabbits by three methods, the

intratesticular, the intracutaneous and the deposition of the virus on a granulating wound. Transfers from 11 patients were made. For syphilis a single transfer was made from a primary genital lesion to rabbits. Fourteen out of 34 rabbits inoculated intratesticularly developed yaws lesions at the inoculation site, the incubation period being 33–108 days. Twelve rabbits inoculated intracutaneously failed to show any lesions. None of 13 rabbits in whom the inoculation of a wound had been attempted became infected. Only intratesticular inoculation succeeded in rabbits. Five monkeys were inoculated from as many patients; definite lesions were produced in 2, questionable lesions in 3 but treponemata were never recovered.

[These results are very disappointing to the authors but they seem satisfied with the rabbit as an experimental animal. This is a pity for obvious reasons and because more work along the lines of the investigations of SCHÖBL is needed.] *H. S. S.*

MIYAO (Isao). **Experimental Inquiry into the Possibility of Transmission of Yaws by Leeches.**—*Philippine Jl. Sci.* 1932. Apr. Vol. 47. No. 4. pp. 463–466.

The experimental evidence concerning the indirect transmission of yaws has been gathered from the available literature and critically discussed by YASUYAMA (*Philippine Jl. Sci.* 1928, Vol. 35, p. 333). Leeches are mentioned as possible vectors. Leeches were allowed to ingest lymph and blood exuding from monkey yaws lesions. At definite intervals, the entire blood content of each leech was taken up in a hypodermic syringe, examined microscopically and injected intradermally into monkeys. Examinations of leech blood revealed spirochaetes in 11 out of 16. Of six monkeys inoculated in none was a lesion produced, though it appeared the spirochaetes would live and possibly multiply in the leech for some short time.

The possibility of transmission by leeches is very remote. *H. S. S.*

HU (Ch'uan-K'Uei) & FRAZIER (Chester N.). **Isolation of *Treponema pallidum* from Juxta-Articular Nodules.**—*Proc. Soc. Experim. Biol. & Med.* 1932. June. Vol. 29. No. 9. pp. 1167–1168.

The authors open with the statement—"The syphilitic nature of the J.A.N. occasionally seen in syphilitic patients is generally accepted principally because of the prompt response of the lesions to arsphenamine therapy." Mention is then made of the usual failure to demonstrate spirochaetes in these lesions by dark-field illumination method or in stained sections. Animal inoculation has been credited with a single success (JESSNER and ROSSIANSKY, *Arch. f. Dermat. u. Syph.* 1930, Vol. 160, p. 224). The authors now report one success in two attempts. The man was infected 12 years before, chancre and positive W.R. and Kahn test. He exhibited "several, small, firm, non-tender nodules in the subcutaneous tissue below both elbows and over the great trochanters." 1·0 cc. of a sterile saline emulsion of an excised nodule was injected into the testicle of two rabbits. An orchitis developed in 10 weeks, W.R. became positive and spirochaetes were demonstrated in juice aspirated from the testicular lesion. [No mention is made of the fact that perhaps yaws is a much commoner cause of J.A.N. and that many lesions presumably when old-standing and fibrous do not respond to treatment by arsenicals.] *H. S. S.*

DE ARAUJO (Eduardo). Caso de bouba observado na Bahia.—Reprinted from *Cultura Med.* 1932. Mar. Vol. 2. No. 3. pp. 130–135. With 1 fig. English summary.

BUTLER (C. S.). The Trouble with "Yaws."—Reprinted from *Amer. Jl. Clin. Path.* 1932. May. Vol. 2. No. 3. pp. 265–269.

STEUDEL (Emil). Zur Klinik und Statistik von Framboesie und Syphilis.—*Arch. f. Schiffs- u. Trop.-Hyg.* 1932. Apr. Vol. 36. No. 4. pp. 243–248.

CLIMATIC BUBO AND LYMPHOGRANULOMA INGUINALE.

FINDLAY (G. M.). **The Relationship of Climatic Bubo and Lymphogranuloma Inguinale.**—*Lancet.* 1932. July 2. pp. 11–13. [16 refs.]

Another link in the chain of evidence proving the identity of the condition called lymphogranuloma inguinale by DURAND, NICOLAS and FAVRE (1913) and climatic bubo. Clinically and pathologically when series of cases were examined there were no differences in the two conditions. FREI (1928) then showed that the intra-dermal reaction which he had introduced for L.I. gave positive results in C.B.; by the use of an antigen prepared from one condition he obtained positive results in the other. In 1930 HELLERSTRÖM and WASSÉN were successful in inoculating monkeys intracerebrally and passaging the virus through a series of animals, experimental work confirmed and carried further by LEVADITI and his colleagues. Others obtained some successes by inguinal inoculation of guineapigs.

G. Marshall Findlay has now shown that, using sterile pus aspirated from softened glands of cases of C.B. infected in Singapore as the intracerebral inoculum in monkeys, a clinical and pathological picture is produced in those animals analogous to that produced by the L.I. antigen.

Characteristic symptoms and histological changes are also produced by intracerebral inoculation of mice as in L.I. Inguinal inoculation into guinea-pigs is followed by a characteristic adenitis as in the cases reported by MEYER, ROSENFELD and ANDERS (1931) using L.I. virus.

The affection can be passaged in monkeys and guineapigs. The virus of C.B. is filtrable as in the case of that of L.I. It remains virulent when preserved in 50 per cent. glycerine in saline at 4°C. for 7 days but not after 14 days. Unlike many neurotropic viruses the concentration of C.B. virus in infected mouse brain does not appear to be very great since dilutions greater than 1 in 1,000 failed to kill.

LEVADITI and co-workers (1932) showed that the serum of L.I. patients possessed virulicidal properties: the same has been shown to be true for cases of C.B. Further the sera of L.I. patients from Paris had similar properties for the virus derived from cases infected in Singapore. *H. S. Stannus.*

GIBSON (P. L.). **The "Non-venereal" or Climatic Bubo. A Clinical Study of a Series of Cases occurring in a Naval Hospital and on Board Ship, with a Discussion of Views of Recent Authorities.**—*Brit. Jl. Ven. Dis.* 1931. Oct. Vol. 7. No. 4. pp. 243–275, & 1932. Jan. Vol. 8. No. 1. pp. 1–47. With 3 charts in text. [53 refs.]

Two rather unnecessarily long articles forming a comprehensive paper on this disease with 27 case histories, discussion of theories in etiology,

pathology, treatment, etc., which unfortunately is now much out of date. The paper was, it is stated in a footnote, received for publication in September, 1930, since when many observations by clinicians, pathologists and research workers have been recorded upon this affection. There is nothing essentially new in the paper except perhaps that the author believes that the prostate and vesiculae may be affected in the disease.

[It seems rather unfortunate that the author should have chosen the term non-venereal bubo as his title, for the disease is commonly communicated by sexual intercourse though not necessarily so, just as both methods of communication occur in syphilis. The author has also fallen into the trap of including the designation granuloma venereum as a synonym for this disease which is now commonly known as lymphogranuloma inguinale, though later he mentions this entirely different condition under differential diagnosis.] *H. S. S.*

LEVADITI (C.), RAVAUT (P.) & SCHOEN (R.). Présence du virus de la maladie de Nicolas et Favre dans les ganglions lymphatiques des singes réceptifs. [**The Presence of L.I. Virus in Glands of Susceptible Monkeys.**]—*C. R. Soc. Biol.* 1932. Apr. 15. Vol. 109. No. 12. pp. 1099–1101.

The presence of the virus of L.I. in the lymphatic glands of monkeys whether inoculated into gland, intra-cerebrally or intra-preputially, has already been demonstrated by HELLERSTRÖM and WASSÉN and the present authors. The last experiments go to show that in monkeys, who do not succumb to intra-glandular or intra-preputial inoculation, the virus may persist for 12, 34 and 111 days. From the monkey thus showing persistence of virus on the 111th day, another gland was removed on the 136th day; an emulsion of this inoculated intra-cerebrally into another test animal proved innocuous. These experiments were carried out on susceptible species, Cynomolgus and Cynocephalus. A *Macacus rhesus*, relatively non-susceptible, after inguinal intra-gland inoculation developed inguinal and axillary adenopathy, but an inguinal gland excised on the 75th day showed no pathological change and an emulsion was non-infective.

H. S. S.

LEVADITI (C.), RAVAUT (P.) & SCHOEN (R.). Nouvelles données sur la maladie de Nicolas et Favre expérimentale du singe et de la souris blanche. [**Experimental L.I. in the Monkey and White Mouse.**]—*C. R. Soc. Biol.* 1932. Apr. 22. Vol. 109. No. 13. pp. 1176–1179.

The results of certain further experiments are here given. The virus is not destroyed by keeping in a vacuum in an ice chest for 12 days. It will not pass through a collodion membrane of three thicknesses under a pressure of 60 mm. Hg. (rate of 1 drop every 2 min. 3 seconds) as will certain other neurotropic viruses. Further experiments were made on white mice. It was shown that after both intraperitoneal and transcranial inoculation the heart blood, liver, spleen, kidney, glands, and brain were infective when used as inocula into other white mice using intracerebral inoculation and submitting these animals to histological examination later. *H. S. S.*

LEVADITI (C.), RAVAUT (P.), & SCHOEN (R.). Propriétés virulicides du sérum des sujets atteints de lymphogranulomatose inguinale (maladie de Nicolas et Favre). Utilisation de la souris comme animal-test. [**Virulicidal Properties of the Serum of L.I. Patients.**] —*C. R. Soc. Biol.* 1932. Apr. 29. Vol. 109. No. 14. pp. 1267–1269.

The authors in previous papers showed that the serum of patients suffering with L.I. possessed virulicidal properties, using intracerebral inoculation of monkeys for the test. In the present paper experiments are reported showing that the test may be made with white mice. Serum from the patient is mixed with an emulsion of virulent brain tissue previously clarified by centrifugation, 1 cc. of each. The mixture is kept for 1½ hours at 37°C. and 17 hours at 5°C. One drop is then inoculated intracerebrally into the white mouse. Controls are inoculated with emulsion plus saline. The mice are killed (they show no symptoms) on the 24th day. All controls showed typical lesions; the others were protected. *H. S. S.*

CAMINOPETROS (J.), PHYLACTOS (A.) & PHOTAKIS (B.). Recherches expérimentales sur la lymphogranulomatose inguinale (maladie de Nicolas et Favre) en Grèce. [**Laboratory Studies in L.I. Infection.**]—*C. R. Soc. Biol.* 1932. June 17. Vol. 110. No. 21. pp. 445–447.

It will be remembered that HELLERSTRÖM and WASSÉN in Sweden and LEVADITI, RAVAUT, LÉPINE and SCHOEN in France found the guineapig and rabbit resistant to the virus of L.I. which was pathogenic for the monkey and white mouse while MEYER, ROSENFELD and ANDERS, FREUND and REISS in Germany worked with a virus which was pathogenic for the first mentioned animals. The authors working in Athens where they discovered 14 typical cases during the past year obtained 2 positive results in 5 attempts to infect monkeys by intracerebral inoculation, with four passages in one case. All attempts to infect guineapigs and rabbits by any method failed. A spermophile (*Citillus citillus*) inoculated intracerebrally with gland pulp remained without symptoms but brain tissue removed after 21 days was virulent for the monkey on intracerebral inoculation. *H. S. S.*

HELLERSTRÖM (S.) & WASSÉN (E.). Studien über die Affinität des Lymphogranuloma inguinale-Virus zu verschiedenen Gewebssystemen beim Affen. [**Affinity of L.I. Virus for Various Tissues in Monkeys.**]—*Ztschr. f. Immunitätsf. u. Experim. Therap.* 1931. Vol. 73. No. 1/2. pp. 110–114.

—— & ——. Weitere Untersuchungen über die Natur des Lymphogranuloma inguinale-Virus. [**The Nature of L.I. Virus.**]—*Ibid.* pp. 114–117.

L.I. virus injected into the abdominal cavity of apes causes a peritonitis with or without exudation characterized by polynuclears, large and small monocytes, red blood cells and endothelioid cells. The exudate will give a Frei skin reaction and is infective for other animals. The mesentery and omentum show the same changes as those seen in human gland disease or meningitis in animals, perivascular infiltration with mononuclear and polynuclear cells. In thus infected apes the blood is virulent thirteen days after infection. Virus

is also present in the spleen after intracerebral and intraperitoneal infection. The virus can pass through the scarified skin without producing a local lesion.

In two tests L.I. virus passed Berkefeld and Chamberland filters. The virus loses its pathogenicity rapidly in ordinary undiluted glycerine. It retains its virulence in portions of brain tissue kept frozen for 22 days. *H. S. S.*

HELLERSTRÖM (Sven). Neuere, wichtigere Ergebnisse auf dem Gebiete der Lymphogranuloma inguinale-Forschung. [**Recent Advances in the Knowledge of L.I.**]—Reprinted from *Zent. f. Haut- u. Geschlechtskr. s. d. Grenzgebiete.* Vol. 40. No. 11/12. pp. 705–716. [2 pages of refs.]

NICOLAU (C. T.). Behandlung des Lymphogranuloma inguinale benignum. [**Treatment.**]—*Klin. Woch.* 1932. June 4. Vol. 11. No. 23. pp. 991–994. [15 refs.]

The first article is an excellent summary upon L.I. up to date ; the second gives notes upon the many forms of treatment which have been tried in that disease, most of them without useful results but no mention is made of the use of T.A.B. vaccine intravenously as advocated by HANSCHELL.

It is impossible to further epitomize these summaries. *H. S. S.*

NICOLAU (C. T.). Lésions histo-pathologiques du lymphogranulome inguinal bénin chez l'homme. [**Histopathology of Benign L.I. in Man.**]—*Bull. et Mém. Soc. Méd. Hôpit. de Bucarest.* 1932. Feb. Vol. 14. No. 2. pp. 39–50. With 8 figs.

——. Recherches expérimentales sur la transmissibilité du lymphogranulome inguinal bénin (Ni-Fa) chez les animaux. [**The Transmission of L.I. to Animals.**]—*Ibid.* pp. 51–58.

——. Considérations sur le traitement du lymphogranulome inguinal bénin. [**The Treatment of L.I.**]—*Ibid.* pp. 58–66. [38 refs.]

The author refers to the observations of other workers and the difficulty of infecting guineapigs and rabbits with the virus of L.I. Nicolau himself in 26 attempts obtained local lesions in 14 guineapigs and generalized lesions in 2. All inoculations of rabbits failed. Using pus from human cases of L.I. inoculated into the inguinal region in guineapigs—the local reaction consisted in a local adenopathy. In the generalized cases iliac, mesenteric, periaortic and peritracheal glands were also affected *or* lung, liver, spleen, kidney, showed lesions *without* lymphatic propagation.

In animals which survived 10–18 days, daily blood examinations revealed a white cell count up to 24,000, due in the earlier days to a polynuclear leucocytosis and later to a lymphocytosis and monocytosis with atypical reticulo-endothelial cells. Temperature often reached 40°C. At necropsy the glands showed the now well recognized changes. The liver was swollen and hyperaemic in patches and showed perivascular proliferative changes of reticulo-endothelium, lymph and plasma cells and typical infiltrations. In the kidney and spleen similar changes were noted, also karyorrhexis and pyknosis of the nuclei of the Malpighian follicles. There was intense hyperaemia of the lungs with subpleural haemorrhages, the pleura was adherent and covered with thick fibrino-purulent exudate. Intraperitoneal and intrapleural

inoculation were also followed by local and generalized infections with typical lesions. The inoculum, after filtration through a Chamberland L, was active on intraperitoneal inoculation.

Gland or other organ emulsion may be used for passaging from animal to animal. Six such passages in guineapigs were made but the impression was gained that the virulence diminished.

Emulsions of glands were used to inoculate dogs in the inguinal regions. A local adenopathy accompanied by fever and leucocytosis reaching a maximum in 3 to 4 days was obtained in 80 per cent. of trials. Five passages in dogs were made. The pathological changes in the glands were similar to those in man and an antigen prepared from a dog's gland gave positive skin test in human cases of L.I. In the last section of the paper the author runs through the multifarious methods of treatment which have been suggested and tried by various workers. *H. S. S.*

MEYER (Kurt) & ANDERS (H. E.). Versuche zur Züchtung des Lymphogranuloma inguinale-Virus. [**Cultivation of L.I. Virus.**]—*Klin. Woch.* 1932. Feb. 20. Vol. 11. No. 8. pp. 318–321. With 1 text fig.

The authors believe they have cultivated the virus of L.I. using the method of H.B. and M. C. MAITLAND (*Lancet*, 1928, II, 596). The culture injected into the inguinal region of guineapigs produced changes in the lymphatic glands comparable with those produced by the injection of material from patients; it also caused a positive Frei reaction in human cases of the disease. *H. S. S.*

KOCH (Franz). Das Lymphogranuloma inguinale. [**Lymphogranuloma inguinale.**]—*Zent. f. Bakt.* I. Abt. Ref. 1932. Feb. 11. Vol. 104. No. 23/24. pp. 529–544. [2 pages of refs.]

A very valuable summary of all the research work which has been carried out by investigators during recent years on Lymphogranuloma inguinale with bibliography—impossible to summarize but necessary to everyone interested in this subject. *H. S. S.*

FISCHER (A. W.) & SCHMIDT-LA BAUME. Rektalstrikturen und Lymphogranuloma inguinale. [**L. I. and Rectal Stricture.**]—*Deut. Med. Woch.* 1932. Apr. 1. Vol. 58. No. 14. pp. 527–529. With 3 text figs. [19 refs.]

After a brief review upon strictures of the rectum of unknown etiology and the recognition by FREI and KOPPEL of the group in which they believe L.I. infection is the specific cause, the authors give the histories of four cases in women coming under their own notice and of one man whose history is worth quoting here :—

34 years old with a previous history of gonorrhoea and syphilis. 5 weeks previous to admission irregular intercourse had taken place. On examination there was a left inguinal adenitis the size of a plum but the skin was not involved. Fever 39°C. A small lesion was present on the fraenum yielding Ducrey's bacillus but no spirochaetes were found. For 10 years patient had suffered a recurring purpura and it was then present associated with thrombopenia. The spleen and liver were enlarged. Frei reaction negative. Later the gland mass became larger and softening took place. 100 cc. sterile pus withdrawn. Symptoms of partial intestinal obstruction came on and this on sigmoidoscopic examination was found to be due to a

mass of glands in abdomen pressing on the wall of the rectum 15 cm. from anal orifice. The mucous membrane was intact but injected. A typhoidal condition was present. Later a positive Frei reaction appeared and in the perineal region lesions consisting of ulcers the size of a penny (Esthiomene) developed which did not contain spirochaetes and healed under treatment with antimony. *H. S. S.*

FEILCHENFELD (Hans). Zur Ätiologie der Elephantiasis vulvae ano-rectalis mit den Rectumstrikturen unter besonderer Berücksichtigung der Lymphogranulomatosis inguinalis. [**Etiology of Elephantiasis Vulvae and Rectal Stricture. Role of L.I.**]—*Med. Klin.* 1932. July 8. Vol. 28. No. 28 (1439). pp. 965–966. [21 refs.]

After a short review of some of the observations by previous writers upon the various theories which have been held in regard to the several conditions known as elephantiasis vulvae, anorectal syphiloma, etc., and rectal stricture the author mentions FREI's finding of positive L.I. skin reactions in such cases, since when an L.I. etiology has been generally accepted.

He gives the histories of one woman and two men with rectal strictures and positive Frei skin tests and then discusses the question whether the stricture is the result of specific L.I. local ulceration in the rectum or is the indirect result of inflammatory changes in the wall of the rectum due to spread from adjoining lymphatic structures. The author thinks there may be direct infection, in contradistinction to BARTHELS and BIBERSTEIN who believe rather in the indirect causation.

H. S. S.

LAEDERICH (L.), LEVADITI (C.), MAMOU (H.) & BEAUCHESNE (H.). Rétrécissement inflammatoire du rectum, forme aberrante de la maladie de Nicolas-Favre. Inoculation au singe positive. [**Inflammatory Rectal Stricture, Aberrant Form of L.I.**]—*Bull. et Mém. Soc. Méd. Hôpit. de Paris.* 1932. July 4. 48th Year. 3rd Ser. No. 23. pp. 1072–1078. With 2 figs.

The authors record a case of inflammatory rectal stricture in a woman, with no other local or general manifestations, which they have proved to be of L.I. origin, both by the skin reaction of FREI and by the method adopted by RAVAUT, LEVADITI, LAMBLING and CACHERA in a case of ulcerative ano-proctitis—namely by the subcutaneous inoculation into a guineapig of a portion of rectal mucous membrane, excision of the gland which developed in the guineapig, emulsification, and intracerebral injection into a monkey, producing thereby in the monkey the typical meningo-encephalitis. *H. S. S.*

LÖHE (H.) & ROSENFELD (H.). Zur Therapie des Lymphogranuloma inguinale. [**Treatment of L.I.**]—*Med. Klin.* 1932. June 24. Vol. 28. No. 26 (1437). pp. 895–897.

Of all the treatments tried in a large series of cases the authors find that the best results are obtained by intra-gluteal injections of solganal in oily suspension, 0·2, 0·3 up to 0·6 cc. of the suspension (2 per cent. for small doses, 20 per cent. for bigger doses) every 5th day at first, then twice weekly, a series of 20 injections with a total of 1½ grams of the gold salt being given. In the pre-softening stage the adenitis clears up and abscess formation is prevented. In later cases with

fistulation the cavities quickly dry up, the effect being noticeable even after 3 or 4 injections. For simple cases a few weeks suffice for treatment; for others a few months may be necessary. Solganal causes a transient albuminuria but is safe in the doses mentioned above, the only contra-indications being kidney disease or dermatitis. It is also unwise to give this preparation if heavy metal antisyphilitic remedies are being administered. In such cases a vaccine treatment is preferred combined with local application of X-rays as has been detailed by others. All other treatments are considered to be of little value. Locally hot applications promote absorption and if softening occurs aspiration of the abscess cavities is advocated, repeated as required.

H. S. S.

GAY-PRIETO (J.). Zur Behandlung der Lymphogranulomatosis inguinalis mit spezifischem Antigen. [**Treatment of L.I. with Specific Antigen.**]—*Dermat. Woch.* 1932. July 16. Vol. 95. No. 29. pp. 1056–1063. With 4 figs.

The author writes of the excellent results he has obtained in the treatment of 3 cases of L.I. by means of intravenous injections of pus antigen diluted 1 : 4 with saline and sterilized by heating at 60°C. for 1 hour on each of three successive days. The antigen or vaccine may be used filtered or unfiltered, the former giving better results but stronger general reactions. For this reason he advises a filtered vaccine for first injection and unfiltered vaccine for subsequent treatments as the reaction is progressively less marked as desensitization takes place. This desensitization in only temporary, for if treatment is discontinued for some time the next injection causes marked general reaction. Dose is from 0·2 cc. to 1·6 cc. at intervals of 2–4 days according to reaction; 4–9 injections were administered. All three cases did well: one early non-suppurative bubo, one suppurative bubo which was aspirated at the same time, and one chronic case which had been incised twice. Healing took place in two weeks.

The same treatment was adopted in two cases of rectal affection due to L.I. virus as proved by Frei's test. In one early case, with infiltration of rectal wall rather than organized stricture, considerable improvement occurred; pain and bloody discharges ceased but the case remains under observation. The second case had had bilateral inguinal buboes five years before and was of long standing with chronic oedema of vulva, condyloma-like perianal growths and fistula. The stricture was doubtless fibrous—a few injections of vaccine caused some focal disturbances and no improvement. The case was handed over to a surgeon.

H. S. S.

FREI (W.). Zur Praxis der Lymphogranuloma-inguinale-Reaktion. [**Frei's Reaction in L. I.**]—*Klin. Woch.* 1932. Mar. 19. Vol. 11. No. 12. pp. 512–514.

An article emphasizing the necessity for care in preparing the antigen and carrying out the test which bears the author's name. Antigen should only be prepared from L.I. patients who are non-tuberculous, not suffering from any venereal disease or history thereof in the past and negative to reactions for syphilis, soft sore and gonorrhoea. The case should be a typical one, the gland to be punctured having undergone softening but the skin should be unaffected.

Contents are aspirated with syringe and large bore needle without drawing blood if possible and introduced into a sterile tube and mixed with 5–6 parts of physiological saline. ½–1 cc. of the mixture is then put up in Jena hard glass ampoules and sealed. These are subjected to 60°C. for two hours and to same temperature for one hour the following day on a water bath. Fresh and heated material is tested for sterility by aerobic and anaerobic culture at room and incubator temperature. It is also examined to prove absence of dead bacteria. Preserve at a low temperature protected from the light. It should give no reaction when tested on normal controls and cases of ulcus molle. If kept over any length of time tests should be repeated every 3 months and after 9 months it should be discarded. Once an ampoule is opened the remains should be thrown away.

For the test 0·1 cc. is injected intracutaneously after alcohol disinfection into suspects and also controls. The result should be read after two days, not before. In a positive result there appears an infiltrated raised inflammatory area ½ cm. in diameter at least, often larger, surrounded by a reddened zone; in the centre of the area, which is dome-shaped rather than flat, a small centre of necrosis is usually found.

A positive reaction may not occur in a L.I. case until the process has involved the skin. In fully developed cases the reaction may fail—the phenomenon of " anergy "—sometimes seen in premenstrual period and in early syphilis but a negative should lead to a further test with another batch of antigen. Skin allergy usually lasts for life, it is believed; but it may be lost after a number of years, a fact which should be remembered in testing some cases of "elephantiasis genitoanorectal."

Excessive reactions may be given by unclean antigen or one containing bacterial products and false reactions may be afforded by injection of other antigens, since the skin of the L.I. patient is hypersensitive to non-specific substances derived from the skin of other subjects. A clear-cut full reaction at the proper time interval must be required. The reaction is then absolutely specific. *H. S. S.*

VALERIO (Americo). A proposito da lymphogranulomatose inguinal.—*Folha Med.* 1932. Mar. 15. Vol. 13. No. 8. pp. 90–91.

WILLOUGHBY (Hugh). Climatic Bubo and Ulcerating Granuloma.—*Jl. Roy. Nav. Med. Serv.* 1932. July. Vol. 18. No. 3. pp. 202–208. With 2 figs.

REVIEWS AND NOTICES.

FISCHL (Viktor) & SCHLOSSBERGER (Hans). **Handbuch der Chemotherapie. Erster Teil: Metallfreie organische Verbindungen.** [Handbook of Chemotherapy. Part I. Non-Metallic Organic Compounds.]—pp. viii+357. 1932. Leipzig: Fischers medizinische Buchhandlung. [Subscription price M.29; after publication price M.34]

In this country, at any rate, the comparatively young science of Chemotherapy has not yet reached the stage when it may be said to suffer from a surfeit of text-books, while even in Germany, the fatherland of Chemotherapy, complete treatises are still comparatively few in number. This is probably due to the fact that to produce a satisfactory text-book of Chemotherapy it is necessary to possess a knowledge of chemistry, pharmacology and experimental pathology with which few, if any, individuals are equipped. In the present instance this difficulty has been largely overcome, for a chemist and an experimental pathologist have combined to write a handbook of Chemotherapy in three volumes, of which the present volume deals with the organic metal-free compounds. Works on Chemotherapy must necessarily be written from either the chemical or the medical point of view, for while the chemist is primarily anxious to know what compounds have shown therapeutic activity, with a view to preparing even more potent derivatives, the medical man desires to obtain information as to the substances which have been found efficacious in a given infection. Though the present work is written more especially from the chemical standpoint the pharmacological properties and clinical applications of each compound are at the same time adequately dealt with. The metal-free organic compounds which have been found to possess chemotherapeutic action form a somewhat heterogeneous collection. As a result, successive chapters deal with such diverse substances as acyclic chlorine compounds, unsaturated fatty acids, simple benzene and naphthalene derivatives, aminoacids, quinoline and quinine derivatives, emetine and allied substances, glucosides, acridine compounds and other dye stuffs. It is perhaps a somewhat depressing reflection to consider how few of these multifarious compounds are of any real value in the treatment of parasitic infections. This must not be taken to imply, however, that the book does not contain a mass of highly valuable information. The correct formula for plasmoquine is now given with more precision: it is shown to be 8-(ω-diethylamino-*iso*pentyl) amino-6-methoxyquinoline and not as was previously thought the N-diethyl-amino*iso*pentyl 8 amino compound. Atebrin, the new antimalarial drug so recently prepared by the I. G. Farbenindustrie of Elberfeld, is described as the dichlorhydrate of an alkylamino-alkylaminoacridine derivative. Its action on malarial schizonts is fully discussed. Much interesting historical matter is also incorporated in the volume. The matrimonial affairs, for instance, of Don Luis Géronimo Fernandez de Cabrera, Bobadilla y Mendoza, 4th Count of Chinchon and sometime viceroy of Peru, are exhaustively dealt with. Countess Anna, who for so long has figured in the history of quinine, despite the fact that she never crossed the sea to South America, must now retire in favour of her successor, the second wife of the Count, Francisca Henriquez de Ribera, whose existence has but recently come to light.

Each chapter of the book is followed by a very complete bibliography; the text is well printed and is singularly free from printer's errors. There is, however, no index. If the high standard of this first volume is maintained the work will most certainly take its place as an authoritative text-book of Chemotherapy. *G. M. Findlay.*

RUSSELL (W. Kerr) [M.D., B.S., etc.]. **Colonic Irrigation.**—pp. ix+191. With 28 text figs. 1932. Edinburgh: E. & S. Livingstone, 16 & 17 Teviot Place. [10s. 6d.]

There is little doubt that many of the ailments from which mankind suffers are due to constipation; hence the honour and wealth which accrued to Beecham, Cockle and Mother Siegel. There is little doubt also that the habit of self-dosing by the laity with aperients is vastly overdone. The author quotes the saying of ALVAREZ: "Why upset twenty-four feet of intestine with a purgative when the material to be removed is in the rectum or sigmoid, within easy reach of a little water?" and this book is largely in the nature of a special plea for lavage or colonic irrigation. If, however, it were indulged in for the numerous conditions in which the author claims that it gives relief or cure the wash-out would become as common as the aperient habit is now.

The chapter on the History of Clysters and Colonic Lavage, from 1500 B.C. to the present time is interesting, this is followed by others on the Anatomy and Physiology of the Colon. The Faeces, their Flora and Parasites, together with chemical examinations, are dealt with in ten pages; consequently the information under this head is far from complete. The statement in the introduction implying that the majority of practitioners diagnose bowel conditions without examining the faeces certainly does not hold good for medical men who practise or have practised in the tropics. On the contrary, they make a rule of examining the faeces whatever the nature of the symptoms.

To state that "tubercle bacilli are only found in the faeces when there is considerable intestinal involvement" is contrary to fact; the author uses a generic name Trichoma both for the flagellate Trichomonas and the metazoon Trichinella. This chapter will need revision in the next issue.

Chapters on the apparatus and methods of administration are full and formidable, ranging from a small squirt of the 18th century and the Higginson syringe of the 19th to the Gymnacolon apparatus (pp. 64, 65), a truly fearsome object like a giant dental chair, the mere sight of which would render the operation superfluous. A list of the substances and solutions which may be used totals 195 and there are formulae of 43 additional solutions.

A final chapter enumerates the conditions benefited by colonic lavage from which we gather that this form of treatment would seem to be almost a panacea. As well as for disorders of the colon it may be used for erythema nodosum, cardiac arrhythmia, renal calculus and many other conditions. Little is said of tropical diseases but the author's experience has indeed been fortunate. Thus, "patients who have been invalided home from the tropics [on account of dysentery] . . . clear up in a surprising way after a short course of lavage" (p. 167), and, more remarkable still, "We have had an opportunity of treating a number of very long-standing cases of sprue; rapid amelioration followed the commencement of colonic irrigation. A short course of treatment invariably (!) sufficed to establish a normal condition of the bowels" (p. 168); this, too, in spite of the fact that the small intestine is generally more involved than the large.

The author is a strong advocate for physical medicine and in this work, which is well printed and well illustrated, he deals very fully with one branch of it. *H. H. S.*